THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—12TH YEAR. SYDNEY: SATURDAY, MARCH 21, 1925. No. 12.

Table of Contents

	PAGE.
ORIGINAL ARTICLES—	
"The Biology of the Cell," by LAUNCELOT HARRISON, B.A., B.Sc.	275
"Recent Advances in Physics and Their Bearing on the Study of Living Matter," by O. U. VONWILLER	277
"Tissue Culture as a Method of Cancer Research," by I. M. MACKERRAS, B.Sc., M.B., Ch.M.	280
"Chronic Irritation and Malignancy," by F. P. SANDES, M.D., Ch.M., B.Sc.	285
REPORTS OF CASES—	
"Varicella Following Herpes Zoster," by GILBERT BROWN, M.B., Ch.B.	286
REVIEWS—	
Basal Metabolism	286
Toxæmias of Pregnancy	286
Clinical Medicine	287
School Inspection and Health	287
The Electro-Cardiogram	288
ANALYTICAL DEPARTMENT—	
"Prescription Glaxo"	288
LEADING ARTICLES—	
The Laboratory and the Clinic	289
CURRENT COMMENT—	
Pernicious Anæmia and Sprue	290
Venous Pulsations	291
ABSTRACTS FROM CURRENT MEDICAL LITERATURE—	
Therapeutics	292
Urology	292
BRITISH MEDICAL ASSOCIATION NEWS—	PAGE.
Scientific	294
Medico-Political	295
MEDICAL SOCIETIES—	
The Alfred Hospital Clinical Society	297
OBITUARY—	
Thomas Clifford Allbutt	298
Eustace Julian Keogh	299
CORRESPONDENCE—	
Postural Tonus	300
Colles's Fracture	300
New South Wales Branch of the British Medical Association	300
Influenza	301
NAVAL AND MILITARY—	
Appointments	301
POST-GRADUATE WORK—	
Post-Graduate Course in Obstetrics	302
PROCEEDINGS OF THE AUSTRALIAN MEDICAL BOARDS—	
Queensland	302
BOOKS RECEIVED	302
MEDICAL APPOINTMENTS VACANT, ETC.	302
MEDICAL APPOINTMENTS: IMPORTANT NOTICE	302
DIARY FOR THE MONTH	302
EDITORIAL NOTICES	302

THE BIOLOGY OF THE CELL.[1]

By LAUNCELOT HARRISON, B.A., B.Sc.,
Professor of Zoology, University of Sydney.

THE changes which have come about in the teaching of zoology during the last twenty years are illustrated perhaps as well as they can be by the very fact that it has been considered appropriate to hold a symposium upon cancer in the lecture theatre of a department of zoology which I, as a professor of zoology, am called upon to open, and in the course of which I shall be followed by two of my research students. The days of pure morphology are passing, although a basis of sound morphology is still an essential in the medical curriculum and a great deal more attention is being given to the functional aspect of zoology. Since the cell is the physiological unit of all organisms, it is but natural that its intensive study should constitute one of the main trends of the new biology which has resulted in the establishment of a new branch of science, that of cytology. The development of the experimental method in biology has created the science of genetics which is concerned ultimately with the nuclear phenomena of cells, as well as discovering methods of cultivating tissues *in vitro* which have proved of the utmost importance in studying the growth and differentiation of cells.

A cell, defined as simply as it can be, is a mass of cytoplasm containing a nucleus. The cytoplasm is mainly composed of protoplasm, the actual structure of which is still unknown to us, owing to the impossibility of obtaining it in a pure state for analysis. Although many structures in the cytoplasm of cells have been described in meticulous detail and although at one time it seemed possible that a study of the so-called Golgi apparatus might prove useful, it cannot be claimed that any very important advance has been made in our knowledge of cytoplasm, except perhaps for certain work of Conklin. Conklin has recorded in the cytoplasm of the egg at fertilization of both molluscs and tunicates differentiated formative materials which give rise to definite parts of the developing embryo. He has even made the same claim with regard to amphibian ova. These observations, if substantiated, are of great theoretical importance, but they do not very deeply concern our present purpose.

When, however, we come to consider the advances which have been made in our knowledge of the cell nucleus, we find that these are many and very important. The broad outlines of the phenomena of karyokinesis have been well enough known for

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on September 11, 1924.

a good many decades, but it is only in recent years that any precise understanding of their significance has been attained. In the first place it has been proved that mitotic division is of almost universal occurrence, although in the protozoa it is much modified in character. Dobell has claimed on this and other grounds that the protozoa must be looked upon as non-cellular and not uni-cellular in nature and there is a good deal of justification for his point of view. In any case it is the metazoan nucleus with which we are more definitely concerned and more particularly with those nuclear phenomena which become apparent during the maturation of germ cells. It is a familiar-fact that each kind of organism has a specific number of chromosomes within the nuclei of its cells. These chromosome numbers have now been determined for a very considerable number both of plants and animals. During 1924 two important additions have been made in this branch of knowledge. Painter, in America, has finally determined the number of chromosomes in man as forty-eight and Agar, in Melbourne, has made the first determination of the number in a marsupial.

Since the number of chromosomes is constant for any species, it follows as a necessary corollary that there must be a lessening of these bodies in the formation of germ cells, as otherwise the constant number would not be maintained. The meiotic division witnesses a change of behaviour on the part of the chromosomes which in ordinary division split longitudinally, half going to each daughter nucleus. In meiosis the chromosomes come together in pairs and it is the double chromosome so formed which divides. If we take the case of man the forty-eight chromosomes unite in pairs to form twenty-four which then split, so that twenty-four pass to each daughter nucleus. Thus both ovum and sperm contain twenty-four chromosomes and fertilization restores the characteristic somatic number. It should be noted that this coupling of the chromosomes is not a haphazard proceeding, but that they exist in definite homologous pairs, one member of which is derived from either parent. The importance of these facts lies in their relation to heredity. Sutton first pointed out in 1902 that this behaviour of the chromosomes in reduction division provided the necessary mechanism to explain the observed facts of Mendelian segregation and his suggestion was very soon confirmed. Following upon this McClung put forward the hypothesis that sex itself was determined by the chromosomes. This too has proved correct, two chromosomes in either sex being concerned in sex determination. In mammals the female sex chromosomes are similar and are called *X*-chromosomes; while the male sex chromosomes are dissimilar and are known as the *X* and *Y* chromosomes. Since the sex chromosomes are homologous pairs, it follows that every ovum will contain an *X* chromosome, while sperms will be of two kinds, half of the total number formed containing an *X* chromosome, the other half a *Y*. It is entirely a matter of chance which kind of sperm effects fertilization, but the *X*-containing sperm automatically produces female and the *Y*-containing sperm male. Later work, particularly that of Crew, has shown that this statement of the method of sex determination does not cover the whole truth, since hormones secreted by the reproductive glands can under certain conditions alter the sex as determined by the chromosomes, but the general statement that sex is determined at fertilization holds good for practically all cases.

The next important observation in this long series of brilliant discoveries was that certain characteristics were limited in a general way to one sex. Congenital colour-blindness in man, for instance, is almost entirely confined to the male, only rarely occurring in the female. This led to the suggestion that the factor for this defect was in some way concerned with a sex chromosome and was the first step in the chromosome theory of heredity. We now know quite well that the defect is located in the *X*-chromosome of an affected male, that it will be passed to all his daughters, who will not themselves be colour-blind as the *X*-chromosome of a normal mother contains the dominant factor for normal vision, but half their sons, on an average, will show the defect. This hint and the discovery of an exceptionally favourable experimental animal in the little vinegar fly, *Drosophila*, started T. H. Morgan and his students at Columbia off upon the wonderful train of experiments which has revolutionized our whole conception of the mechanism of heredity and has proved beyond any possibility of doubt that the bulk of our physical and mental characteristics are determined by *loci* occupying definite positions along the length of definite chromosomes and that each of our forty-eight chromosomes represents a catalogue of characters determined for us at conception, containing a quantative half of the total available parental heritage, the quality of which is a matter of chance.

The discovery of radium or helium, the announcement of a theory of relativity and other such things come with a dramatic suddenness which is absent from biological discovery. In the latter we have a slow approach through a series of steps, each important, but with an importance not fully realized until the culmination of the series is realized. The world at large knows Madame Curie and Einstein, but is still in a blissful state of ignorance about T. H. Morgan. Yet it seems likely that Morgan's work on heredity will ultimately rank as high as any previous discovery in science. The details of human inheritance have not yet been worked out, but sufficient information has already been obtained to indicate the far-reaching importance for human welfare of this branch of cell biology when it becomes better known.

A full exposition of tissue culture methods and results is to follow, so there is no need for me to anticipate this. But I may perhaps be allowed to say a few words about one aspect of cell physiology. In the early embryonic life of any organism there are stages in which all the cells of the body are alike or undifferentiated. Such stages, however, do not persist for very long, for a process of differentiation soon sets in and a majority of the cells becomes modified in various ways to form tissue

cells of different kinds. Those which remain unmodified, give origin to the gonads. Differentiation is accompanied by a loss of potentiality, but it has been found that under certain circumstances cells can dedifferentiate, that is to say revert to what is practically an embryonic condition. This happens when they are removed from the influences which normally control them. A considerable body of experimental workers is engaged in studying the nature of differentiation and dedifferentiation and of the influences which control these processes and new facts are daily being brought to light. A full understanding of the functions of the normal cell is a necessary pre-requisite to the study of abnormal cell behaviour and the best hope for such an understanding lies in the hands of the experimentalists.

Cancer is a problem in cell biology. The cells of malignant growths appear to originate from dedifferentiated tissue cells which have by some means not at present understood escaped from normal control and inhibition. When we attain to a full knowledge of the nature of normal control, we shall be in a much better position for controlling the abnormal. Whether cancer research will ever become concerned with the heredity mechanism of the cell is a moot point, but it is conceivable that though cancer itself is not heritable, some predisposing condition may be and a further knowledge of the mechanism of human heredity may cast light upon this aspect of the problem. In the short time at my disposal it has not been possible to do more than touch lightly upon one or two branches of cell biology and that in a very elementary way; but I hope that my few words will serve some purpose as an introduction to the more serious contributions which follow.

RECENT ADVANCES IN PHYSICS AND THEIR BEARING ON THE STUDY OF LIVING MATTER.[1]

By O. U. Vonwiller,
Professor of Physics, University of Sydney.

The epoch-making discoveries of the last thirty years in connexion with the nature of matter have resulted in a wide extension of our knowledge in every branch of physics and already have proved of benefit in many applications depending on our fuller acquaintance with the inner structure of atoms. In living matter, as far as we know, all the laws of physics and chemistry hold, so that it is reasonable to suppose that an appreciation of the recent advances in physics will likewise prove of great value in the attempt to explain the processes taking place in living matter and perhaps enable us in some measure to control or modify these processes.

The Atom.

From the discovery of the electron and of X-rays and radio activity in the concluding years of the nineteenth century, there has followed a sequence of investigations which enables us to-day to make a picture of the atom which we feel must be essentially correct, though, of course, it is far from complete, because each step forward brings fresh difficulties before us.

Briefly, we know that atoms of all kinds are built up of two constituents: electrons, tiny, negatively charged particles and protons, yet smaller positively charged particles, the charges in each being numerically the same. The mass of a proton is about 1,850 times that of an electron, so that the mass of an atom is due mainly to the protons. Uncharged atoms contain equal numbers of each; the hydrogen atom consists of one proton and one electron, the helium atom of four of each, the oxygen atom contains sixteen of each, the "atomic mass" being the number of protons (or of electrons in the uncharged atom). Fractional values of "atomic weights" are usually due to the substance being a mixture of two or more isotopes; thus chlorine consists of two varieties of atomic mass: 35 and 37; but chemically indistinguishable. In some cases, notably hydrogen (1.008), the fractional value requires some other explanation.

The Nature of Light.

Closely connected with the modern view of the atom we have the question of the nature of light. A theory in support of which there seems to be overwhelming evidence, the *"quantum"* theory, states that light energy is built up of definite units or *quanta*, the *quantum* for light of any kind being proportional to the frequency, so that when light in the extreme violet end of the spectrum is emitted or absorbed, the amount of energy involved is an integral multiple of a unit or *quantum* nearly twice as great as the *quantum* for light in the extreme red, while the *quantum* for X-rays is many times greater corresponding to the higher frequency. In an X-ray tube the hardest rays excited have a frequency for which the *quantum* corresponds with the kinetic energy of the electrons, the stopping of which causes the emission of the rays and the converse effect holds, the kinetic energy of the electrons emitted, when X-rays fall on matter, at most equals the *quantum* for X-rays; similar relations hold between the maximum kinetic energy of electrons given off and the *quantum* of the light in the photo-electric effect, the emission of electrons from metals upon the incidence of light (usually ultra-violet).

Nuclear Protons and Extra-Nuclear Electrons.

The atom can be divided into regions. There is a central portion, the nucleus, the constituents of which are comparatively closely packed; it contains all the protons and except in the case of hydrogen some of the electrons, so that nearly the whole mass is in the nucleus. The "atomic number" is the difference between the number of protons and of nuclear electrons and is, of course, proportional to the positive charge on the nucleus. In a radio-active substance changes in the nuclei of the atoms occur spontaneously and, on bombardment by α rays, an occasional disintegration of a nucleus is produced in atoms of some of the other elements, but generally the nuclear portion of atoms is outside our control.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on September 11, 1924.

Outside the nucleus at distances comparatively great are the remaining electrons; they revolve round the nucleus in approximately elliptical orbits somewhat as planets revolve round the sun. According to the theory elaborated by Bohr only certain orbits can be occupied by such electrons instead of any orbit as would be expected on the classical theory of attraction. Certain simple relations hold between the amounts of energy associated with an electron when moving in various orbits and by supplying the appropriate amount of energy an electron can be moved from one orbit to another or, if it return, it can give out an equal amount in the form of light, the frequency of which satisfies the *quantum* law being proportional to the energy involved in the change of orbits. According to Bohr atoms only emit light when an electron is thus changing its orbit, moving from one of high to one of low energy or when an electron moves from right outside the atom to one of the unoccupied orbits.

In all but the lightest atoms the extra-nuclear electrons can be divided into groups. Thus in the case of calcium we have twenty such electrons; there are two innermost orbits, each occupied by an electron and characterized by the "*quantum* number" one; then there is a group of eight orbits of "*quantum* number" two and outside these a group of eight orbits of "*quantum* number" three; each of these is normally occupied by one electron; the two remaining electrons occupy two outer orbits of "*quantum* number" four. Any of these electrons may be removed from the atom by the supply of sufficient energy, the amount required being greatest for the orbits of lowest "*quantum* number" and least for the orbits of highest "*quantum* number" or an electron may be transferred from an inner orbit to a possible orbit of higher "*quantum* number" five, six, seven *et cetera* normally unoccupied, the energy required for this being less than that needed completely to remove it. The energy needed for such removal or transfer of an electron may be supplied through a collision with some rapidly-moving electron or charged atom as in the case of an electrical discharge through a gas or from light incident on the matter, provided that the frequency is such that the *quantum* is not less than the energy required to produce the change. The most stable state of the atom is that in which the inner orbits are all occupied as indicated above; if by the supply of energy a change is produced, the atom soon comes back to this normal state by an electron moving back to the vacant orbit; this return is accompanied by the emission of a *quantum* of light, the various lines of the spectrum corresponding with movements of an electron between the various pairs of orbits or from outside to the various orbits.

"Sheath" Electrons.

The outermost group of electrons in the normal atom is called the "sheath." The number of electrons in it ranges from one to eight in different elements. These are the most readily removed electrons and in cases in which the number in the "sheath" is small, very little energy is needed to detach at least one. In metals it appears that as a result of the inter-atomic impacts at ordinary temperatures, some are detached, so that in the solid there are numerous positively charged atoms with free or temporarily free electrons moving in the intervening space; the high conductivity of metals is due to these free electrons.

The "sheath" electrons are involved in the chemical properties of the elements. Atoms with a small number in the "sheath" can readily lose these and are electro-positive, the remaining atom having a positive charge proportional to the number lost, while atoms with a large number in the "sheath" readily take and hold an extra electron or electrons to make the total number eight, acquiring a corresponding negative charge. We see this illustrated in the charges on the ions in an electrolyte; for example, when a crystal of sodium chloride is dissolved in water sodium and chlorine ions are formed, the former consisting of sodium atoms which have lost the single electron present in the "sheath" of the neutral sodium atom, while the chlorine ions have acquired each an extra ion completing the "sheath" of eight, the uncharged chlorine atom having a "sheath" with seven electrons. The atom of copper has two electrons in its "sheath," so in solutions of cupric salts we find that the copper ions have a charge double that in sodium ions, corresponding to the loss of two electrons.

The laws of chemical combination, the property known as valency and so forth, can be seen to fit in well with the idea here indicated, the tendency of the "sheath" electrons to form a group of eight by addition or loss. In stable molecules consisting of two or more atoms the "sheath" of each atom consists of eight, this being brought about by pairs of electrons being shared by two atoms, this sharing being the link holding them together; thus the oxygen atom has six electrons in its "sheath" and in the molecule of oxygen four electrons are common to the "sheaths" of each atom, so that each has a "sheath" of eight; similarly, in the chlorine molecule two electrons are shared by the two "sheaths," so that each "sheath" consists of eight, the number in the neutral atom being seven. The inert character of gases, such as neon and argon, is due to the "sheath" being complete, containing eight electrons in the neutral atom, so that here electrons are removed only by supply of a comparatively large amount of energy, as in an electrical discharge through the gas.

The energy required to remove an electron from one of the innermost orbits of an atom increases with the atomic number of the element and, the *quantum* relation holding, the frequency of the light emitted in the return of an electron increases in like manner. In the heavier atoms X-rays are emitted when electrons return to inner orbits, the frequency for corresponding transfers being greatest for the atoms of greatest atomic number.

The changes produced in matter by the incidence of light are due primarily to the removal of electrons from atoms in which the light energy is absorbed. In the case of X-rays and γ rays for which the *quantum* is large, one of the inner electrons may be removed or if the *quantum* is absorbed

by an easily detached outer electron, this may acquire considerable kinetic energy enabling it to free outer electrons from other atoms; with ultra-violet light only the more easily released outer electrons are detached. In compound substances in which the atoms forming a molecule are held together by the arrangement of the "sheath" electrons, the removal of one of these might well cause an instability resulting in a new grouping or a breaking up of the molecule. If the prime effect of X-rays is a removal of one of the deep-seated electrons, the result may be the same because outer ones tend to move into any vacant interior orbit. Such chemical changes may occur in living or in non-living matter; in the former where changes are continually occurring and a balance is maintained between various physical processes, a disturbance such as that suggested may result in very considerable modification.

Living Matter.

In the cells of any organism we are largely concerned from the standpoint of the physicist with aqueous solutions of various materials. The complexity of the substances, the small quantities and the ever varying conditions make the cell very unfavourable for rigorous experiment and discussion, but we do know that just as with non-living matter the principle of the conservation of energy is true, that the potential energy of the system tends towards a minimum value, that the laws of solutions and of surfaces of separation of different materials hold. For example, in such liquids diffusion occurs tending to equalize the concentration of any solute throughout. If two solutions are separated by a membrane permeable to water, but not to the solutes, we have the phenomenon of osmosis, a transfer of the water across the membrane until the molecular concentration is the same on each side or until there is developed a sufficiently great difference of pressure, the osmotic pressure, to prevent further transfer. At the same time we have surface tension effects Associated with each surface separating two media is potential energy proportional in amount to the area of the surface and depending in value upon the materials and on conditions such as temperature. In a solution if, as is usually the case, the surface tension decreases with increased concentration, there is concentration at the surface greater than in the bulk of the liquid, because in this way the potential energy is reduced. This effect, adsorption, is in opposition to the process of diffusion and we have a balance between them. There will likewise be a tendency for changes of shape to occur, making the total surface energy a minimum. Further complications arise owing to electrical effects if the solutions are electrolytes. In these there is dissociation, breaking up of the solute into positive and negative ions, the degree of dissociation depending on the concentration, on the temperature and on the presence of other salts. The adsorption effects may differ for the two kinds of ions, so that there results a tendency for a surface to become charged through the greater concentration of ions of one sign. Electric forces then arise resulting in the attraction of ions of the opposite sign and when a balance is obtained, there is formed a double layer of electrification often found at the surface of separation of two liquids or of liquid and gas or liquid and solid. Similar effects may arise in diffusion through membranes; owing to differences in size or other causes the membrane may be permeable to ions of one sign and not to those of the other, so that again electric forces are brought into play.

With non-living matter, in solutions of various kinds, liquids containing solids in suspension, solutions separated by semi-permeable membranes, these various effects exist. In any particular case sooner or later there is attained a condition of statistical equilibrium when the distribution of particles of various kinds in the system is steady under the influence of the various forces involved. In this state in which the concentration may vary from point to point in a solution, differences of pressure may be developed on either side of a membrane, strongly electrified layers may exist at boundaries of materials with intense electric fields in their immediate neighbourhood, the equilibrium arrangement is that for which the total potential energy, taking all kinds into account, is a minimum. If a change is made, such as a supply of heat at some part or the addition of some constituent to a liquid, the balance is upset and changes take place until a new state of equilibrium is established. Sometimes a comparatively insignificant factor produces changes of very great degree before the new steady condition is attained as in the coagulation of a colloid.

In living matter consisting of materials such as those just considered, it is likely that we never have a steady state of affairs, as changes take place continuously in the various parts of the cells in connexion with the processes of life. Under normal conditions the necessary accommodation can be made to the varying conditions, the readjustments can be made sufficiently rapidly, but under abnormal conditions this may no longer be the case. It is not difficult to picture an apparently small disturbing factor upsetting things very badly and we can understand why in some cases X-rays or ultra-violet light or similar agency which primarily causes simply the emission of electrons from a very few of the atoms present, may produce very serious results through the resulting chemical changes or the alterations in local concentrations of ions destroying the balance between the various physical and chemical processes involved in the existence and working of the cell.

To describe completely the happenings in living cells and to understand exactly the effect of a disturbing factor, such as X-rays, so that the results of some definite treatment may be predicted with accuracy or so that the treatment necessary to produce some desired change may be specified, are certainly far beyond us at present. We do know, however, something of the factors to be considered in these problems and can see that we have at our disposal agencies which are likely to prove of immense value when we know how to use them.

The plan of attack most likely to insure an increase of knowledge leading to improved methods of treatment of disease by X-rays and similar radiations, seems to consist of systematic and rigorous experiments carried out on suitable non-living and living matter by physicists and chemists, biologists and physiologists all in close cooperation. From a well-organized campaign on such lines we might confidently expect some definite advance in a reasonable time.

TISSUE CULTURE AS A METHOD OF CANCER RESEARCH.[1]

By I. M. Mackerras, B.Sc., M.B., Ch.M.,
John Coutts and Science Research Scholar in Zoology in the University of Sydney.

Owing to the arrival of certain recent papers since this paper was read, the subject matter has been slightly modified, more especially in the direction of giving a somewhat fuller state of the problem of dedifferentiation. The main object of the communication, however, which was to give a brief description of one method of biological investigation and to indicate its application to some aspects of the study of neoplasia, remains the same.

General Considerations.

In 1910 Ross Harrison[33] first cultivated pieces of the neural tube of tadpoles in lymph from the dorsal lymph sac of the adult frog and watched the axones of the nerve cells growing out into the medium. At the present day a vast number of tissues, embryonic, adult and pathological, from many vertebrates and some invertebrates can be cultured at will, measured accurately and subjected to controlled environmental alterations, an enormous technical advance which is largely due to the work of Carrel and his collaborators at the Rockefeller Institute. The following are amongst the more important of these technical developments:

1. The discovery of the growth-promoting action of embryonic tissue juices, whether homospecific[1] or heterospecific.[2]

2. The use of a prepared fibrin as a scaffolding, thus eliminating the necessity for the presence of serum.[3]

3. The development[4] of the flask method of cultivating large quantities of tissue, while avoiding contamination during manipulations and the use of a medium consisting of a fibrin basis and a fluid part which can be changed daily and altered at will. Under these conditions cultures can be maintained for periods varying from twenty to thirty-five days without sub-culturing and there is sufficient fluid to be tested for substances secreted by the growing cells.

4. The isolation of pure cultures of various types of cells, fibroblasts, cartilage cells, various epithelia, leucocytes and tumour cells.

If a small piece of embryonic tissue be transferred under aseptic conditions to a drop of plasma on a cover slip, the plasma clots immediately and after a variable latent period cells will be found extending into the clot and undergoing active mitosis. After some days growth ceases and the cells die from the toxic effect of the accumulated metabolites unless they are transferred to fresh medium, when growth will continue as before. Eventually the strain dies out. A similar type of growth occurs in a purely saline medium and the curve of growth which is S-shaped, represents the residual growth energy of the tissue, the important point being that the cells are utilizing only such food as was present in the tissue at the moment of explantation and are not synthesizing any material from the medium.[5] Under these conditions embryonic and tumour cells will proliferate actively, adult tissues slightly or not at all.[6] The whole question of the residual growth activity and its dependence on the inherent growth energy of tissues has been investigated by Carrel[7] who found that the inherent growth energy of a tissue is a function *inter alia* of its previous history, for example a strain of fibroblasts from a ten-day chick embryo grew more extensively and for a longer time than one from a seventeen-day embryo. The difference between the growth of tumour and normal cells in a non-nutritive medium is probably in part at any rate due to the differences in their previous history.

When, however, a saline extract of embryonic tissues is added to the medium, the sequence of events is very different. The rate of growth is greatly accelerated, sub-culturing can be continued indefinitely and the curve of growth instead of being S-shaped, is a parabola which may be produced indefinitely. By the use of such extracts Ebeling has been able to keep a strain of chick fibroblasts proliferating actively from January 17, 1912, to the present day. When reporting on its completion of ten years life *in vitro*,[8] he stated that the tissue had been sub-cultured by division in half 1,860 times and that more than 30,000 cultures had been derived from it during that time. Obviously the increase in mass has been enormous and it must have been able to synthesize into protoplasm some substances which are present in embryonic extracts but not in plasma or saline solution. A very important fact was that in a medium of constant composition the rate of growth was constant over long periods of time and that it responded readily to modifications in the composition of the medium by modifications in its rate of proliferation. Such a culture is in fact "a physiological reagent for detecting in serum and other fluids the presence of substances promoting or inhibiting cell multiplication."

The whole question of growth and its relation to the nutritive nature of the medium has been very ably summarized by Carrel[9] in a recent address to which the reader is referred for further details on this very important subject and also for a magnificent demonstration of the application of quantitative methods in biology.

Factors Influencing Growth Rate.

Since most cultures are made in clotted plasma, it is important to have a clear understanding of

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on September 11, 1924.

the action of serum on cells *in vitro*. Two somewhat unexpected results have come from the study of this question by Carrel and Ebeling,[5] [10] firstly that serum is absolutely non-nutritive to fixed tissue cells *in vitro* and secondly that serum exerts an inhibitory action on cell division, the degree of inhibition being proportional to the age of the animal from which the serum was taken. There are apparently two substances present in serum, one thermo-labile and growth promoting, the other thermo-stable and growth inhibiting. While fairly evenly balanced in the young animal the former gradually decreases and the latter increases as age advances. These observations bring us a step nearer to an understanding of the slowing down and final cessation of developmental processes which occur as an animal reaches maturity.

A long series of investigations, however, have shown that certain substances, called trephones by Carrel, have the property of being both nutritive to fixed tissue cells and able to overcome the inhibitory action of serum. The earlier work[1] showed that such growth activating substances are present in extracts of many tissues in varying degree, most of all in extracts of embryonic tissues, to a slightly lesser extent in sarcoma and adult spleen and still less in kidney, heart and other organs. Walton[11] has analysed the effects of various tissue extracts and finds that, while liver extract is inhibitory to the growth of both the connective tissues and to the parenchyma of various organs including liver, extracts of other organs all activate the growth of connective tissue and have a varying effect on the parenchyma of different organs inhibiting some and promoting the growth of others. Drew[12] confirmed the earlier work, but found that it was necessary to incubate the extracts of adult tissues for one hour at 37° C. in order to develope their growth-promoting action; these he called autolytic extracts. He also made the very important observation that the amount of growth-promoting substance present in extracts of malignant tumours was directly proportional to their malignancy *in vivo*, with the natural corollary that the rate of growth of a malignant tumour in a non-nutritive medium was proportional to its malignancy.

Carrel and Ebeling turned their attention to the mobile body cells and demonstrated that trephones occur in extracts of leucocytes, in exudates containing many leucocytes and also that they are secreted into the medium by leucocytes living *in vitro*. Leucocytes, in contra-distinction to the fixed tissue cells, will proliferate in serum and they alter the serum in some way that makes it a suitable pabulum for fixed tissue cells. Their work demonstrates beyond reasonable doubt the important function, previously suspected on other grounds, of leucocytes in transforming substances brought by the blood into material which can be assimilated by the fixed tissues.[13] [14] [15] [16] [17] While fibroblasts were used in the earlier work, Ebeling[18] has shown that leucocytic trephones act in a similar way on epithelial tissues.

What is the chemical nature of trephones, whether there are two kinds of substances at work, one which is a source of food and another which stimulates cell division, or whether appropriate nourishment in adequate quantity is all that is necessary to determine active proliferation and what relation the trephones bear to the materials used by cells as a source of energy and of specific secretion are questions which must be left for future investigations to answer. Certainly there are considerable qualitative differences between different extracts. It also remains to be explained how tumours come to contain much more growth-promoting (or stimulating?) substances than normal tissues. The round cell reaction commonly seen in tumours would in part account for this difference, but it hardly seems all sufficient.

Whatever may be the gaps and they are big gaps in our knowledge, the importance of what is already known can hardly be over-estimated in view of the light that is thrown on the pathogenesis of certain abnormal conditions met with *in vivo*. Wherever there is histolysis and an accumulation of leucocytes, there will be a liberation of trephones in sufficient quantities to overcome the inhibitory action of the serum and set up a proliferation both of the stroma and of the parenchyma. This, according to Carrel, is the mechanism of the cellular response to the action of any irritant *in vivo*. If the action of the irritant is limited, histolysis ceases, the leucocytes are removed, the serum can reassert its inhibitory influence and the lesion heals; if on the other hand the irritative process is long continued and trephones are persistently liberated, we get an overgrowth, a hyperplasia both of stroma and parenchyma such as is characteristic of various chronic inflammatory conditions. If we extend these conclusions a little further and also consider the fact that the inherent growth energy of a tissue is in part a function of its previous history, one may reasonably ask whether long continued life under such conditions as are met with in chronic inflammation and in the constant presence of trephones may not be an important factor in determining that access of growth energy which is characteristic of malignant cells. And might not a slight difference in the intensity of such a process of trephone liberation combined with an increased disturbance of tissue relations have a considerable influence in changing cells whose nature has been altered by their previous history from a condition of chronic hyperplasia to one of malignant activity?

Before passing on to the question of dedifferentiation, I may mention here certain work which may throw some light on the results of other workers who are attacking the cancer problem from other points of view. In the first place Murphy and his co-workers[19] have found that lymphocytes suspended in serum from irradiated animals increased by 15% to 30% in two hours and mitotic figures were frequently seen, whereas the count decreased when the suspension was made in the serum of a non-irradiated animal and mitosis was only seen once in many experiments. Serum exposed to the action of X-rays *in vitro* is devoid of any stimulating action. Strangeways[20] finds that irradiation of the cells of tissue cultures produces modifications of the chromosomes leading finally to fragmenta-

tion and death; injury within variable limits produces permanent alteration which persists through an indefinite number of generations. Secondly, Mendéléeff[21] found that calcium ions stimulate the growth of epithelium *in vitro*, whereas potassium ions only permit a short survival and zinc ions are highly toxic. Lastly, Drew[6] observed that sarcoma cells secrete substances *in vitro* which are toxic to cells from the same sarcoma and are completely specific in that they do not affect the growth of any other kinds of tissue; he was not able to use these substances for the destruction of sarcomatous masses *in vivo*, as they were rapidly destroyed when injected into the living animal. This is interesting in view of the fact that round-cell sarcomata show areas of necrosis more frequently than any other tumours.

Dedifferentiation.

The outstanding correlated phenomena of malignant disease are firstly the great growth energy of malignant cells, secondly their physiological and morphological loss of specialization and thirdly their disturbed relation to surrounding tissues as shown by their power to infiltrate. A certain amount of light has been thrown on the first of these questions by the work which has been reviewed in the previous section and it remains to consider here what information can be obtained about the second and third.

When small pieces of tissue are explanted into a clotted medium, after a variable time cells grow out from the tissue mass, epithelium as a flat sheet, connective tissue as a dense mass of reticulated branching cells and leucocytes as isolated clumps and individuals showing no tendency to form any coherent tissue. These cells, while retaining their fundamental nature as epithelium or connective tissue, do not when growing out of relation with other tissues form highly organized structures, but proliferate as a tissue which is of an apparently lowly and unspecialized type. Carrel[9] describes the appearance of a pure culture of thyreoid epithelial cells in the following words: "Sometimes they form acini with colloidal material in the centre, generally they are more or less irregularly spread in the coagulum and some drops of colloid substances with their characteristic appearance can be seen within the cells or near them in the medium." An examination of his figure, which I take to be of a typical part of the culture, shows a sheet of cells which have very little resemblance to fully functional, differentiated thyreoid epithelium, no acini are shown and it is difficult to make out the presence of any secretion which must be small in amount and irregularly formed. In fact pure cultures of epithelial cells of which several types have been grown,[9] [12] [18] [22] seem to bear no closer relation to their parent cells than do the cells of rapidly-growing carcinomata to the tissues from which they originated, and they differ one from another in no greater degree than do the more malignant types of carcinomata growing from different tissues. It must be noted that Champy[23] [24] believes that after some time *in vitro* all tissues reverted to a single primitive type "*comparables aux cellules d'un blastoderme jeune*," but nobody, as far as I am aware, has been able to confirm his observations in their entirety. In fact the bulk of evidence, especially that derived from regrafting experiments, goes to show that despite this apparent loss of differentiation in pure culture the cells remain fundamentally the same, thyreoid cells never being capable of becoming anything other than thyreoid and even cancer cells retaining their carcinomatous nature. There is no real evidence that the cells of tissue cultures ever revert so far to an undifferentiated condition that they could redifferentiate into something other than the type of cell from which they took origin. The mesenchymal group of cells form an apparent exception to this statement in that Lewis[25] noted that mesothelium and mesenchyme only represent a different arrangement of the same type of cell; and Carrel and Ebeling[13] observed large mononuclear cells differentiating into cells resembling fibroblasts: but one must remember that there is considerable evidence from other sources for the pluripotency of mesenchymal cells and for the close relationship between fibroblasts, mesothelium and the large wandering cells.

With these facts before us we may pass on to a consideration of the vexed question of dedifferentiation. There has been a good deal of disagreement amongst different workers, the American school absolutely denying its occurrence in tissue culture, while Drew in England and Champy in France maintain that it is universal in pure cultures. A careful examination of the published work and especially of the figures leads one to think that much of the difference of opinion is due to a difference in the meaning of the word as used by various authors. For example, Fischer[26] described the metamorphosis of a pure strain of cartilage cells into large, round cells growing in a sheet like an epithelial tissue and resembling not at all the appearance of fully formed cartilage cells *in vivo*. He stated that dedifferentiation did not occur, presumably because there was no change into a blastodermic or even into a primitive mesenchymal type of cell. European workers would consider this as a striking example of dedifferentiation because there was an obvious loss of functional and morphological specialization. Precisely the same thing may be said of many other pure cultures. If the term dedifferentiation be limited to apply only to a return to a totipotent or even to a pluripotent condition, then it very probably does not occur in tissue culture and some other term must be found to indicate the loss of functional and morphological differentiation, without necessarily any loss of unipotency, which certainly does occur in tissue culture. It is not apparent from their writings that either Drew or Carleton,[27] who give a useful summary of the question, have had the question of potency clearly before their minds when they speak of dedifferentiation in tissue culture. Mr. P. D. F. Murray has suggested to me that the term dedifferentiation be reserved for the return to a pluripotent or totipotent condition and that one might use the word semi-dedifferentiation for the condition found in tissue culture and also

in malignant tumours, a word that emphasizes the probability that the conditions are merely steps in a continuous process.

Given then that a process which we may call semi-dedifferentiation, occurs in tissue culture and that it is at any rate analogous with the physiological and morphological changes found in tumours, we may ask what are the factors underlying this process. The subject is still but little understood, but two factors stand out clearly as having an important influence. These are: (*i.*) Differentiation of cells is a function of their relation to cells of other tissues and to each other. (*ii.*) It is also a function of the rate of proliferation. Cells whose rate of division is slowed down, tend to differentiate.

In favour of the first proposition there is so much evidence that it may be said to be conclusively established. Champy[28] first called attention to the fact that epithelium grown in relation with connective tissue remained differentiated and this observation was greatly extended by later workers, notably by Drew,[12] who showed that kidney and alveolar mammary carcinoma cells grew in pure cultures as undifferentiated sheets of cells, but immediately became organized into tubules on the one hand and acini on the other if connective tissue were added to the culture. Similarly pure cultures of squamous epithelium formed keratine when connective tissue was added. Of the pure culture of thyreoid cells mentioned above Carrel says: "When pure cultures of fibroblasts are added to thyroid tissue, the fibroblasts soon surround the thyroid epithelium which organizes into a small gland showing acini filled with colloidal substance." Ebeling and Fischer[29] have obtained similar results with mixed cultures of pure strains of epithelium and fibroblasts. Champy and Coca's work[30] is also of considerable interest in this connexion. They took a polypoid *adenoma uteri* the distal part of which had become malignant, and cultivated pieces of tissue from the adenomatous base. The gland cells, when growing *in vitro* out of normal relation with the stroma, lost their differentiation and assumed precisely the appearance of the cells from the malignant tip. Certain of these experiments indicate too that there is a quantitative relation, a delicate balance between the amount of antagonistic tissue present and the degree of differentiation of the parenchymatous cells, and also that connective tissues have a definite influence on the division rate of parenchymatous cells.

The evidence for the second conclusion is almost equally strong. Champy[24] early noticed that the more rapidly cells divided, the more quickly they "dedifferentiated." Fischer[31] pointed out that epithelial cells in old cultures tend to form tubules or to keratinize in the case of skin, when proliferation is beginning to be inhibited by the accumulation of toxic metabolites and Ebeling[18] observed that the addition of inhibitory serum to a pure culture of epithelium from the iris of a chick embryo caused the cells to secrete large quantities of black pigment as soon as the inhibiting action made itself felt. Strangeways[20] emphasized the fact that loss of specialized characters is a necessary accompaniment of mitosis and that at the end of mitosis a cell has two courses open to it; it may either divide again or it may redifferentiate, but it cannot do both together.

The outstanding feature of these experiments is that one may produce varying degrees of semi-dedifferentiation simply by varying the extent of operation of certain factors and may obtain anything from a mass of unspecialized cells to what is practically a complete organ. When one compares these findings with the fact that a continuous series may be obtained linking certain chronic inflammatory conditions with some malignant tumours *in vivo*, one is forced to consider seriously whether the difference between chronic inflammation and neoplasia is not merely one of degree rather than of specific nature, whether in fact the phenomena of neoplasia are not in many cases simply those of chronic inflammation carried to excess.

If the influence of trephones be correlated with the effects of division rate on differentiation and with the effects of disturbed tissue relations both on growth rate and on differentiation, then we obtain a very clear picture of the processes of inflammation, whether acute or chronic and a rather better understanding of the biology of tumour cells. That these are some of the factors underlying the phenomena of malignant growth is reasonably sure, but that they are not the whole story is even more certain as will be shown in the following paragraphs.

That the resemblance between pure cultures of normal cells and malignant cells *in vivo* is not really as close as histological appearances would lead us to believe is shown by the fact that their loss of differentiation is not irreversible, as is apparently the case with tumours *in vivo*, and that there is a fundamental difference between normal cells and tumour cells, which persists right throughout their life in tissue culture, is clearly demonstrated by their behaviour on being grafted back into the animal body. Strangeways[20] has succeeded in getting grafts of "dedifferentiated" normal tissues to take and states that they redifferentiate and form small masses which are later completely reabsorbed. Drew[12] failed to get successful grafts of normal tissues but found that cells from an adeno-carcinoma which had lost in culture what differentiation they had originally possessed, redifferentiated and formed not the kind of mass that Strangeways obtained with normal tissues, but the original type of tumour. Fischer[32] obtained malignant tumours by grafting six months old cultures of sarcoma. In general terms tumour cells remain unipotent for their particular type of growth and normal cells unipotent for normality throughout their life *in vitro*. It is this permanent nature of the malignant characters of tumour cells which remains at present entirely unexplained.

Another very striking difference between malignant cells and normal cells was noted by Fischer.[32] He kept sarcoma cells thriving *in vitro* for six months by growing them in conjunction with small pieces of muscle which they infiltrated and destroyed, utilizing the muscle substance as food. Under these conditions they were quite able to main-

tain indefinite growth in the absence of embryonic extract. There is no evidence that normal cells can use living muscle as food or can maintain growth indefinitely *in vitro* in the absence of an activating extract.

Summary and Conclusions.

Tissue culture has proved a most fruitful field of research and has thrown a considerable light on several phases of cellular activity, some of which are of great interest to the investigator of malignant disease.

The growth-promoting action of trephones and the influence of the previous history of a cell on its growth energy may have an influence in starting a cell on a malignant career.

The effects of division rate and of the relation of tissues to each other on the morphological and physiological specialization of cells help to explain the histological picture presented by tumours.

These investigations have also served to isolate certain definite problems connected with neoplasia. How do tumours come to contain more growth-promoting substance than normal tissues? What special characteristic enables tumour cells to destroy muscle cells *in vitro* and use them as food and how have they acquired it? What is the explanation of the permanency of the malignant condition? These questions are difficult enough to answer at present, but the future may bring fresh improvements in technique which will make their solution possible.

Finally, it must be remembered that this method of biological study is still a recent acquisition. Seeing that the results already obtained are of considerable interest, may we not hope that the work of the future will be of still greater value?

References.

(1) A. Carrel: "Artificial Activation of the Growth *in Vitro* of Connective Tissue," *Journal of Experimental Medicine*, 1913, Volume XVII., page 14.

(2) A. Carrel and A. H. Ebeling: "Action on Fibroblasts of Extracts of Homologous and Heterologous Tissues," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 499.

(3) A. H. Ebeling: "Fibrin and Serum as a Culture Medium," *Journal of Experimental Medicine*, 1921, Volume XXXIII., page 641.

(4) A. Carrel: "A Method for the Physiological Study of Cells *in Vitro*," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 407.

(5) A. Carrel and A. H. Ebeling: "Survival and Growth of Fibroblasts *in Vitro*," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 486.

(6) A. H. Drew: "A Comparative Study of Normal and Malignant Tissues Grown in Artificial Culture," *British Journal of Experimental Pathology*, 1922, Volume III., page 20.

(7) A. Carrel: "Measurement of the Inherent Growth Energy of Tissues," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 521.

(8) A. H. Ebeling: "A Ten Year Old Strain of Fibroblasts," *Journal of Experimental Medicine*, 1922, Volume XXXV., page 755.

(9) A. Carrel: "An Address on the Method of Tissue Culture and its Bearing on Pathological Problems," *The British Medical Journal*, July 26, 1924, page 140.

(10) A. Carrel and A. H. Ebeling: "Antagonistic Growth Principles of Serum and their Relation to Old Age," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 419.

(11) A. J. Walton: "The Effect of Various Tissue Extracts on the Growth of Adult Mammalian Cells *in Vitro*," *Journal of Experimental Medicine*, 1914, Volume XX., page 554.

(12) A. H. Drew: "Growth and Differentiation in Tissue Culture," *British Journal of Experimental Pathology*, 1923, Volume IV., page 46.

(13) A Carrel and A. H. Ebeling: "Pure Cultures of Large Mononuclear Leucocytes," *Journal of Experimental Medicine*, 1922, Volume XXXVI., page 365.

(14) A. Carrel and A. H. Ebeling: "Leucocytic Secretions," *Journal of Experimental Medicine*, 1922, Volume XXXVI., page 645.

(15) A. Carrel and A. H. Ebeling: "Action of Serum on Lymphocytes *in Vitro*," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 513.

(16) A. Carrel: "Growth-Promoting Function of Leucocytes," *Journal of Experimental Medicine*, 1922, Volume XXXVI., page 385.

(17) A Carrel: "Leukocytic Trephones," *The Journal of the American Medical Association*, January 26, 1924, page 255.

(18) A. H. Ebeling: "*Cultures Pures d'Epithelium Proliferant in Vitro depuis dix-huit Mois*," *Comptes Rendus de la Société de Biologie*, 1924, *Volume* XC., *page* 562.

(19) J. B. Murphy, J. Liu Heng and E. Sturm: "Studies on X-Ray Effects—IX.: The Action of Serum from X-Rayed Animals on Lymphoid Cells *in Vitro*," *Journal of Experimental Medicine*, 1922, Volume XXXV., page 373.

(20) T. S. P. Strangeways: "Tissue Culture in Relation to Growth and Differentiation," 1924.

(21) P. Menéléeff: "*L'Influence des Ions Ca et des autres Ions Metalliques sur la Croissance des Tissus Vivants in Vitro*," *Comptes rendus de la Société de Biologie*, 1924, *Volume* XC., *page* 985.

(22) A. Fischer: "A Three Months' Old Strain of Epithelium," *Journal of Experimental Medicine*, 1922, Volume XXXVI., page 367.

(23) C. Champy: "*Sur les Phénomènes Cytologiques qui s'Observent dans les Tissus Cultivés en dehors de l'Organisme*," *Bibligraphie d'Anatomie*, 1913, *Volume* XXXIII., *page* 184.

(24) C. Champy: "*Quelques Résultats de la Méthode de Culture des Tissus*," *Archives de Zoologie Expérimentale et Générale*, (*Notes et Révue*), 1924, page 42.

(25) W. H. Lewis: "Mesenchyme and Mesothelium," *Journal of Experimental Medicine*, 1923, Volume XXXVIII., page 257.

(26) A. Fischer: "A Pure Strain of Cartilage Cells," *Journal of Experimental Medicine*, 1922, Volume XXXVI., page 393.

(27) H. M. Carleton: "Tissue Culture: A Critical Summary," *British Journal of Experimental Biology*, 1923, Volume I., page 131.

(28) C. Champy: "*La Présence d'un Tissu Antagoniste Maintient la Différentiation d'un Tissu Cultivé en dehors de l'Organisme*," *Comptes Rendus de la Société de Biologie*, 1914, *Volume* LXXVI., *page* 31.

(29) A. H. Ebeling and A. Fischer: "Mixed Cultures of Pure Strains of Fibroblasts and Epithelial Cells," *Journal of Experimental Medicine*, 1922, Volume XXXVI., page 284.

(30) C. Champy *et* F. Coca: "*Pathologie de Cancer et Culture des Tissus*," *Journal de Physiologie et de Pathologie, Générale*, 1919, *Volume* XVIII., *page* 549.

(31) A. Fischer: "The Differentiation and Keratinization of Epithelium *in Vitro*," *Journal of Experimental Medicine*, 1924, Volume XXXIX., page 585.

(32) A. Fischer: "*Sur la Culture Indefiniment Prolongée en dehors de l'Organisme de Cellules Provenant de Tumeurs Malignes*," *Comptes Rendus de la Société de Biologie*, 1924, *Volume* XC., *page* 1181.

(33) R. Harrison: "Outgrowth of the Nerve Fibre in Tissue Culture," *Journal of Experimental Zoology*, 1910, Volume IX., page 786.

CHRONIC IRRITATION AND MALIGNANCY.[1]

The Value of Bio-Physical Research into the Relations Between the Reaction to Injury and the Genesis of Malignant Disease.

By F. P. Sandes, M.D., Ch.M., B.Sc.,
Professor of Surgery, University of Sydney; Honorary Surgeon, Royal Prince Alfred Hospital, Sydney.

Normal nutrition in living things depends upon the preservation of a protoplasmic balance finely adjusted, but capable of variation within certain limits. In the absence of any knowledge of the quality of "vitalism" we are compelled to study the conditions subserving this balance by regarding living cells as mechanisms which we are able to analyse into constituent parts. By comparison with similarly analysed mechanisms we can arrive at an understanding, as yet incomplete, of some of the more important factors in the vital activity of cells. If we regard living cells as complex thermo-dynamic machines or systems, never in absolute equilibrium, the physical and chemical processes occurring in them can only receive their ultimate explanations when we have a more perfect knowledge than we have at present of the arrangement of electrons in atoms and molecules.

The chief physical factors in the maintenance of protoplasmic balance are:

(i.) Surface action involving the consideration of the behaviour of electrons at the surfaces and boundaries of cells and in reference to their colloid constituents. Intimately connected with such considerations are the problems of molecular concentration and orientation at surfaces and basement membranes whose permeability may thereby be explained. (ii.) Electrolytic action and ionization.

The chemical factors of importance in maintaining protoplasmic balance are (i.) water, partly dissociated in hydrogen and hydroxyl ions, (ii.) amino-acids, (iii.) salts of sodium, potassium, calcium and magnesium, especially the phosphates, carbonates and chlorides.

By the interaction of these two classes of factors, chemical and physical, the hydrogen ion concentration which is the measure of the fine adjustment of the balance, is altered in accordance with the needs of cell activity.

One of the most characteristic endowments of living things is the capacity to react to injurious stimuli, whether these are mechanical or chemical (including toxins) or physical, such as heat and radiation. In acute inflammatory lesions violent disturbances of protoplasmic balance occur. In chronic inflammation these disturbances are of smaller degree and greater duration, whilst in malignant disease they are in many cases more insidious and still more prolonged. Is there some common factor at work in the production of these varying conditions resulting from injury or irritation?

In many physiological and pathological processes in the human being the potassium atom plays an important part. Next to the hydrogen ion the potassium ion has the greatest mobility. The potassium atom is peculiar in that it is the atom of lowest atomic weight with radio-active properties. So far as is known it is the only one in the human body that gives off electrons in a manner analagous to that of radium or uranium. It enters into intimate relationship with calcium, sodium and probably magnesium in maintaining the functional efficiency of protoplasm. MacCallum's researches have shown that it tends to be concentrated at the boundaries of cells and near basement membranes and suggest that its distribution is capable of variation during cell activity. It is, as it were, a "key" in the industries of cell life and the coarse adjustment of which the hydrogen ion concentration is the fine, in the maintenance of cell function. Further by reason of its emitted radiation it is a potent mechanical factor in energizing cell constituents so that "vital" phenomena are produced.

To go a step further, I would suggest that in the presence of long continued irritation the reaction of cells to injurious stimuli and the pathological consequences arising therefrom are largely due to disturbance of their potassium distribution and metabolism and that in certain types of malignant growth the same cause is at work. It is well known that physical agencies, such as radiations of different wave lengths, are capable of creating and curing inflammatory and malignant conditions. The cell is a reversible engine in this respect and the potassium and hydrogen ion concentrations are the most likely to be affected. The isolation of the specific wave lengths that cause various pathological phenomena bids fair to be accomplished by cooperation between the physicist and the biologist. The study of the effect of radiations upon the constituent atoms of living cells is an essential part of the science of bio-physics. I would draw your attention to the fact that the physicist has, by his development of the science of spectroscopy, placed in our hands instruments for the investigation of atomic and molecular architecture a million times more accurate and sensitive than are the most powerful microscopes in examining the details of cell structure. Let us apply our ingenuity to using these for the purposes of bio-physical research in the hope that perhaps the day will come when the surgeon will lay aside his scalpel and resort to the treatment of chronic inflammatory and malignant disease by radiation apparatus of special design in the attempt to realize the older clinicians' ideal of curing *"cito, tuto et jucunde."*

[1] Being an abstract of a paper read at a meeting of the New South Wales Branch of the British Medical Association on September 11, 1924.

Reports of Cases.

VARICELLA FOLLOWING HERPES ZOSTER.

By Gilbert Brown, M.B., Ch.B. (Liverpool),
Adelaide, South Australia.

During the last two or three years the medical journals have published reports of varicella infection following contact with a patient suffering from *herpes zoster*. Little attempt, however, has been made to prove the absence of direct contact with other persons suffering from varicella. The following case appears to exclude this possibility as the patient was in quarantine for another disease.

I.B. (my own son), *ætatis* seven years, was kept away from school on October 30, 1924, on account of a cold. On November 10 he became affected by mild whooping cough and was quarantined in the garden. His companions were restricted to three children, G.R., *ætatis* five years, L.R., *ætatis* three and a half years, from whom he had contracted whooping cough, and A. McG., *ætatis* three and a half years, who had suffered from it two years previously.

On November 13 the last child was examined on account of pain in the back and left leg. Typical *herpes zoster* of the left side of the sacrum and left thigh was found and the child put to bed.

On November 26 I was called in to see his brother and sister, C.L.McG., *ætatis* eight years, and June McG., *ætatis* seven months. They both manifested a copious varicella rash.

The following morning, November 27, my son I.B. exhibited a similar eruption.

G.R. and L.R. had suffered from this disease two years previously and were not affected.

A sister in the other family, Jean McG., *ætatis* ten years, had also had it while away from home four years before and was not affected. The incubation period of varicella is ten to fifteen days which corresponds to the period between the occurrence of the *herpes zoster* and that of the cases of varicella.

There was no case at the school attended by C.L.McG. and Jean McG. nor was there any other case in the district so far as could be ascertained.

From this and other cases reported there seems strong evidence that both *herpes zoster* and varicella may be different manifestations of the same disease.

It is difficult to understand why the same organism may give rise to either an acute specific disease of the nervous system with a localization in the ganglia of the posterior roots or an acute contagious disease characterized by a generalized eruption.

Reviews.

BASAL METABOLISM.

Lusk in the third (1917) edition of his book, "The Science of Nutrition," declared that there would be no more editions. Lusk's book has had no rival and it still remains the greatest book of its kind. In many ways the little book by Dr. W. S. McCann, of the Johns Hopkins Hospital Medical Clinic, "Calorimetry in Medicine," is like a continuation of the older book.[1] It can be said to carry on the review of the progress of knowledge of metabolism on its dynamical side from the date of the last edition of Lusk's book. It is carried out in the same personal, critical way and by a practical and thoroughly competent physiologist.

This is high praise. Dr. McCann has done a necessary work and done it well. The work involved in the production of a book like this, small as it looks when printed, is prodigious. A critical review embodying no less than tnree hundred and four references to original papers cannot be written well without much time and much thought. It is a very different thing from a mere non-critical digest.

After a few pages of introduction, dealing with history, methods and apparatus, the author discusses the subject of basal metabolism, a term which comparatively few medical men have yet learned to understand, sometimes because they have found no good explanation in the books at their disposal. The relation of metabolism to surface area is explained very well. Dr. McCann then deals with the effect of various factors on basal metabolism. As we should expect, great attention is directed to the relationship between disease of the thyreoid gland and changes in basal metabolism.

Amongst the list of the newer observations in the field of metabolism we note one here. He mentions that Lusk has shown recently (in 1922) that the increase of metabolism caused by the specific dynamic action of protein is not available for work production. The heat evolved by this extra metabolism is available (as was shown by Rubner), in substitution for the extra heat otherwise induced by environmental cold. This observation of Lusk's adds one more weighty argument against the use of a high protein diet in hot climates. It tends to make the individual hotter and makes an extra demand on the mechanism for getting rid of heat. In other words, he has to sweat more. The energy requirement for work is superimposed upon the metabolism induced by the specific dynamic action of protein.

Dr. McCann is emphatically of opinion that calorimetry is greatly misunderstood by clinicians and it is evident that he disapproves of the "stunt" culturists very much indeed. He states in his preface that the least valuable of the contributions of calorimetry to medicine is that by which it is best known to the majority of physicians, namely, the use of calorimetry in diagnosis. This he reiterates over and over again in his book. He adds on page 62:

> The pathological states in which the greatest deviations from average normal are found, are those of the thyroid gland, fevers and diseases of the hæmopoietic system. Smaller variations have been observed in a great number of diseases. These facts should make it clear that the diagnostic value of metabolism determinations is no greater than that of a total leucocyte count.
>
> If the basal metabolism is determined by the most accurate technique, under rigidly controlled conditions, a deviation from the average normal can be properly interpreted only in the light of the most thorough and painstaking clinical study of the case. In the last analysis a diagnosis must rest upon the clinical observations.
>
> As an unbiassed objective method of evaluating the results of therapeutic measures in thyroid disease, especially as a means of controlling the treatment of hypothyroidism, basal metabolism determinations are invaluable.

Again, on page 82 he writes:

> In those conditions which produce marked abnormalities of the basal metabolism, its determination for diagnostic purposes is usually superfluous, though it remains of value as a measure of the severity of hyper- or hypothyroidism and is thus useful as an index of the effectiveness of treatment in these two conditions. . . The possibilities of technical errors in the determinations are greatly multiplied by the widespread use by inexperienced observers of simple forms of apparatus lacking adequate checks and controls. . . Taking all things into consideration, the diagnostic value of basal metabolism tests may be said to be very slight.

These are timely remarks.

TOXÆMIAS OF PREGNANCY.

In the preface to "Modern Views on the Toxæmias of Pregnancy," O. L. W. de Wesselow and J. M. Wyatt state that: "This small volume is an attempt to gather together the more important facts which are at present scattered

[1] "Calorimetry in Medicine: Medicine Monographs," by William S. McCann, Associate Professor of Medicine, Associate Physician, Johns Hopkins Hospital; Volume IV.; 1924. Baltimore: Williams and Wilkins Company. Royal 8vo., pp. 98. Price: $2.25, post paid.

in numerous papers, into a connected whole. The conclusions drawn are to some extent provisional and may with increasing knowledge require revision."

The authors throughout the whole nine chapters into which the book[1] is divided, are most careful in their estimation of the value of the various newer methods used in diagnosis and prognosis and they emphasize the importance of the older clinical methods which have stood the test of time. For example, in the pre-eclamptic state they rely chiefly on the blood pressure chart and the daily excretion of urine in coming to a decision when to terminate pregnancy. They state that the clinical estimations are of value in the differential diagnosis between eclampsia and allied conditions and a chronic renal failure.

We note with pleasure the following statement: "There is strong evidence that the pre-eclamptic state and eclampsia are not accompanied by any appreciable degree of acidosis." The administration of sodium bicarbonate in these conditions is therefore definitely contra-indicated. There are very few statements in the book to which any exception can be taken.

We have much pleasure in recommending this work to the attention of anyone who wants a simple comprehensive survey of the modern work on this subject.

CLINICAL MEDICINE.

THE first volume of "The Practical Medicine Series" consists of extracts of articles from many of the leading journals of the world. It has to do with infectious diseases, diseases of the chest, of the blood and of the digestive system.[2] Comments have been added by the editors when they have thought fit to do so. The selection has been made with much care and skill and the book is a valuable work of reference for clinicians. The papers have not been condensed too much and the author's arguments can be readily followed. A few papers which have been given a place, are criticized somewhat adversely and attention is called to their purely speculative nature. This is an excellent plan as it serves to focus the attention of busy practitioners on some of the current teaching which passes for truth only until it is carefully and dispassionately reviewed in the light of known facts.

This work can be confidently recommended to those who wish to keep abreast of current work without the labour of reading many journals and also to those who need some guidance as to the value of published papers.

SCHOOL INSPECTION AND HEALTH.

THERE has recently been published the second edition of "Medical and Sanitary Inspection of Schools," by Dr. S. W. Newmayer.[3] In his preface the author states that his object "is to give knowledge rather than information," a somewhat curious distinction; fortunately his treatise offers its readers a considerable amount of each.

The subject matter is well treated in a very readable manner and bears evidence that the author is thoroughly acquainted with it in its many aspects.

Part I. on "Administration" is somewhat too detailed to be of general interest and a considerable part of the information given is unsuited to Australian conditions. The same may be said of Part II., in which the author deals chiefly with "School Buildings and Grounds." A number of useful suggestions, however, may be culled from the sections on school furniture, school housekeeping, the drinking vessels and so on.

Parts III. and IV., devoted to "Communicable Diseases" and "Physical Defects" respectively, are particularly valuable from the point of view of medical inspectors who are new to the work, of school nurses and of teachers.

The detection of infection in schools, exclusion and the signs and symptoms of disease are simply and succinctly set out and an excellent table of rules for isolation and exclusion from school is given on page 206. These rules are in use in New York State and might well be adopted throughout Australia; each State in the Commonwealth has some such rules. Uniformity would be an advantage and those named could hardly be improved.

In Part IV. there are many points of interest that call for comment; lack of space, however, allows of but one, that upon the methods advocated in the section upon "Teeth" under the heading "A Last Resort to Avoid Extraction." The writer believes that alveolar abscesses (which as all observers know are common in the mouths of neglected children and even of some who would not be placed in that category) are due very greatly "to the lodgment and protection which a partially enclosed carious cavity affords to pus-producing bacteria—it is the mechanical requisite—therefore, with this removed, we have destroyed one of the essentials necessary for the production of pus, and happily, as with all our work, some trust must be given to Nature's support, so does it follow here." He points out that if the carious tooth is removed above the gum by means of a revolving corundum stone, the non-infective roots are left to absorb gradually without injuring the underlying permanent tooth. At the same time the loss of space caused by extraction is prevented. It would be worth trying this method on a large scale, were it proved to be as successful as is claimed. A *via media* would exist between the conflicting schools of thought, one of which advocates the extraction of all temporary carious teeth, while the other refuses to extract any.

Part V., which is concerned with "The Health of the Teachers," is short and to the point. There must be entire agreement with the dictum on page 343 that "those frequently in contact and closely observing the work in class cannot but be impressed with the apathy of teachers for their own physical welfare." Figures are given which show carelessness about such easily recognized and yet important defects as carious teeth and poor vision. The indifference of the teachers results in a similar attitude on the part of education authorities who fail, therefore, to provide luncheon and rest rooms, who overcrowd class rooms and who permit much clogging of the educational machines and waste of nervous energy on the part of teachers by not arranging for the grading of children in accordance with their mental capacity, or for the provision of special classes.

In Part VI. the author deals with "Mentality" and in comparatively small space describes the uses and advantages of group and individual tests, the classification and treatment of mentally retarded children. He draws special attention to the care necessary to exclude or remedy such possible causes as malnutrition, defective sight and defective hearing before a child may finally be called retarded.

Part VII. treats of such other subjects as "Medical Inspection by Teachers and Nurses," "Rural School Medical Inspection" and so forth. The section on "Child Labour: Medical Inspection" is especially good. Australia is behind both Great Britain and parts of America in the protection of adolescent workers. No child should be allowed to take up work when leaving school at the age of fourteen without a certificate from a doctor setting forth his standard of physical fitness and suitability for the proposed work. Provision should also be made for at least an annual examination up to the age of eighteen.

The objectives given on page 445 under the heading "The Future of Health Supervision" are such as must claim the hearty assent of all who are interested in pre-

[1] "Modern Views on the Toxæmias of Pregnancy," by O. L. V. de Wesselow. M.B. (Oxon.), F.R.C.P., and J. M. Wyatt, M.B. (London), F.R.C.P.; Modern Medical Monographs, Edited by Hugh Maclean, M.D., D.Sc.; 1924. London: Constable and Company, Limited. Sydney: Angus and Robertson, Limited. Demy 8vo., pp. 99.

[2] "The Practical Medicine Series, Comprising Eight Volumes on the Year's Progress in Medicine and Surgery," under the General Editorial Charge of Charles L. Mix, A.M., M.D.; Volume I.: "Infectious Diseases, Diseases of the Chest, of the Blood and Digestive System"; 1924. Chicago: The Year Book Publishers. Crown 8vo., pp. 736, with illustrations.

[3] "Medical and Sanitary Inspection of Schools, by S. W. Newmayer, A.B., M.D.; 1924. Philadelphia and New York: Lea and Febiger; Post 8vo., pp. 462, with 79 engravings and six plates. Price: $4.00.

ventive medicine. Among them are: the elimination of certain communicable diseases (diphtheria, small-pox, scarlet fever, measles, whooping cough); the disappearance of malnutrition; the correction of physical defects before the child is admitted to school when such defects will interfere with education; adequate treatment centres for teeth, tonsils and eyes.

The present unnecessary waste of time, money and energy caused by the distribution of house visitation by tuberculosis and school nurses, infant welfare nurses and welfare visitors will be avoided by the proper training of one nurse to undertake all these duties. She will then be assigned a small area in which she will know and visit each family and will so be able to guide and maintain them in the paths of personal and commercial hygiene.

In conclusion, it is possible to recommend this book to those for whom it was written, health officers, medical practitioners, nurses, teachers. For novices it will prove an invaluable introduction to more elaborate and scientific works, while to even the most experienced workers in the field ideas and suggestions are presented which merit attention and consideration.

THE ELECTRO-CARDIOGRAM.

"The Clinical Aspects of the Electro-Cardiogram," by Harold G. B. Pardee, is a monograph which places in a concise form the present day knowledge of the interpretations and prognostic significance of the curves obtained by the use of this instrument.[1]

The normal curve is fully described and also the normal variations, that is such variations as can be considered normal. The curves of one individual are as distinct from the curves of another individual as are their thumb prints.

Certain curves which are generally recognized as abnormal, are well considered and the author shows that he has a wide knowledge of the subject with which he deals. The interpretations of abnormal curves which rest on experimental evidence, are clear and definite. These are curves relating to auricular fibillation, flutter, auriculo-ventricular block, bundle block and so forth.

It is in the interpretations of curves for which little experimental evidence can be produced, that the author's conclusions may not always be accepted.

As always happens, however, in every branch of medicine the clinician with a variety of patients whose conditions he must diagnose and whom he must treat, goes further into what might be called clinical speculation as to the causes of disease than the facts of experimental evidence may perhaps justify. The author associates certain abnormal but not unusual curves with specific cardiac lesions and cardiac diseases.

An example of this is found on page 81. We are shown curves with a peculiarity of the T wave inasmuch as the S—T interval shows an upward convexity. As in certain of these cases there is found at autopsy a recent occlusion of a branch of the coronary artery, the abnormal T wave is associated with the lesion and indicative of the lesion.

Such a conclusion is a speculation, but may be even legitimate. These, however, are minor points. A detailed description of the electro-cardiograph is given and the method of its operation. The instrument described is the model used in America, the Williams Hindle electro-cardiograph. The principle involved is the same as in the Cambridge electro-cardiograph which is used in England.

Though criticism has been levelled at certain details, the book contains all that it is necessary to know about the clinical interpretations of the electro-cardiogram. Some theoretical considerations are added which are essential for the due appreciation of curves.

The book can be well recommended.

[1] "Clinical Aspects of the Electrocardiogram," by Harold E. B. Pardee, M.D.; 1924. New York: Paul B. Hoeber, Inc.; Demy 8vo., pp. 222, with 56 illustrations. Price: $4.00.

Analytical Department.

"PRESCRIPTION GLAXO."

In October, 1921, we published a report on the result of an investigation carried out by our inspector into the manufacture of "Glaxo" and of a series of analyses of this product. In that report it was pointed out that during the preparation a process of standardization is introduced before the milk is dried, the butter fat content is determined and bicarbonate of soda and lactose are added. It was found that powdered "Glaxo" when suspended in eight times its volume of water yielded a mixture with a somewhat high protein component, a relatively low carbo-hydrate component and an average fat component. Joseph Nathan and Company, Limited, have introduced a modification of "Glaxo," manufactured precisely as ordinary "Glaxo," but standardized in such a manner as to approach the usually accepted average constitution of human milk. This new preparation is known as "Prescription Glaxo" or "Humanized Glaxo."

We have subjected "Prescription Glaxo" to a series of analyses and have scrutinized the claims made by the manufacturers for it. The samples tested were presumably of recent preparation; in consequence we have had no opportunity of ascertaining the length of time this product will remain unchanged in its hermetically sealed tins. Unfortunately the date of manufacture is not stamped on the tin. We hold that this should be done, so that the consumer may be aware if the retailer attempts to sell dried milk that has been kept in stock for an unduly long time. Each tin carries a label on which is printed the directions for diluting "Prescription Glaxo" according to the age of the infant. The method of measurement is somewhat crude. It consists of a metal measure corresponding to the standard teaspoon and tablespoon. The capacity of the tablespoon is approximately fourteen cubic centimetres and may, therefore, be accepted as correct. Rough experiment revealed that when the powdered "Glaxo" is measured in it, the weight is 5.498 grammes if trouble be taken to fill the measure with care and to remove a slight excess with a light straight instrument such as a knitting needle. When the spoon measure was filled in a somewhat haphazard fashion and the excess brushed off without care, as much as 6.751 grammes were collected, while a quick movement to expel the excess led to a reduction to 4.5 grammes. The manufacturers call attention to the possibility of variations in quantity if the measurement is careless, but it is unlikely that the ordinary mother will be able to exercise sufficient care and skill to obtain quantities approximating 5.5 grammes.

For an infant of between one and two weeks the manufacturers recommend one part of "Prescription Glaxo" and three parts of water. When the product was mixed in these proportions with hot, recently boiled water and allowed to cool, a good emulsion was obtained. After one or two hours the fats separated and tended to adhere to the glass or other container. Analyses carried out with freshly made emulsions yielded the following:

Fat	4.06%
Protein	1.77%
Carbo-hydrate (lactose)	8.30%
Ash	0.56%
Water	85.31%
Total solids	14.69%
Solids not fat	10.6%

The claim of the manufacturers is therefore justified; "Prescription Glaxo" has a composition closely approximating that of the usual departmental standard of human milk. The lactose content is relatively high, as is the fat content.

This preparation may, therefore, be recommended for use when mother's milk is not available. It is a high-class preparation made from first quality milk under excellent conditions. The user should exercise great care in measuring the required amount of powder and in avoiding a separation of the fat from the suspension.

The Medical Journal of Australia

SATURDAY, MARCH 21, 1925.

The Laboratory and the Clinic.

Sir Archibald Garrod recently pointed out that there was a danger that the fission between the laboratory workers and the clinicians may go too far. He recognized the inevitable differentiation between these two groups of workers, but deplored that the practitioner who is attracted to the laboratory on account of its more exact methods was apt to look too closely at the disease and too little at the patient. As long as curative medicine continues there will be a large demand for general and special practitioners and the majority of doctors after graduation will elect to supply this demand. Only a few are attracted to the investigational aspect of medicine and of these a substantial proportion is not prepared to adopt laboratory work as a career because of the small rewards offered. Sir Archibald Garrod's two groups are of unequal size; the danger to which he alludes, is due to the fact that the laboratory worker has a different outlook and is not prepared to waste time in fighting for facilities to control his work in the clinic. Progress in medicine now-a-days depends very largely on laboratory research. The exact methods of experimental inquiry have been responsible for the greater part of our knowledge of disease processes. It is no one's duty to pay for research work and as a result this work is carried out for its own sake more often than for the sake of remuneration. That there is a real danger in the divorce of laboratory research from clinical observation may be admitted, but the cause must be sought in the system rather than in any narrowness of the point of view of the laboratory worker.

Research work demands keen powers of observation, a fine imagination, untiring application and much general information. These are relatively rare qualities and since progress in knowledge depends on them, no one possessed of them should be allowed to waste his or her gifts. The special qualities of a competent clinician are of a different nature and should be nurtured and husbanded very carefully. They, too, are valuable gifts. But it should be recognized that there is little risk of a waste of the special endowment for a clinician.

The remedy for the defect to which Sir Archibald Garrod has referred, is the creation of a career for laboratory workers. The value of the work is admitted; there is little or no difference of opinion concerning the relative infrequency of an aptitude for scientific research. The natural corollary may, therefore, be conceded that it is unjustifiable to permit a man or woman with this special aptitude to be forced into general practice on account of the pecuniary advantage accruing. The problem is therefore one of pounds, shillings and pence. In the old world and in America research has been endowed on a liberal scale by private individuals who realize that there is no better way of "unloading" riches than by supporting medical and other scientific research work. Viscount Iveagh's contribution to the Lister Institute was over a quarter of a million pounds sterling. Monsieur Osiris gave over a million pounds sterling to the Pasteur Institute. Mr. John D. Rockefeller has showered over thirty-five million pounds sterling on research work. So far no large donation to medical research has been made in Australia. The main purpose of a fund for research is the payment of salaries and therefore the capital sum required must be large.

The second method that obtains in England, is the ear-marking of certain moneys provided by Parliament for this purpose. It will be remembered that originally the Medical Research Committee received one penny for each insured person for the so-called "tuberculosis benefit." This money was used by the Insurance Commissioners for research in the problems connected with tuberculosis and other diseases. Since 1921 the Privy Council took over this work and the Medical Research Council receives an annual grant from Parliament. Whether it would be wise to press for a considerable subsidy for medical research out of consolidated revenue is a debateable question. If this expedient were adopted, it would be necessary to provide that no departmental control of research would be

exercised. The research worker must have much freedom and must be allowed to give his imagination full play.

If the wealthy citizens can be induced to invest a half of a million pounds sterling in Australia in medical research, it will be advisable for the three Universities with medical schools to appoint a research council to coordinate and guide research work and to induce those with aptitude to select the laboratory as a field of activity. At the same time the same authority could grant the laboratory worker facilities for controlling his work in the wards of the teaching hospitals. The time is ripe for the adequate endowment of careers in medical research.

Current Comment.

PERNICIOUS ANÆMIA AND SPRUE.

MANY observers have drawn attention to the close resemblance that may be presented by the clinical picture of a patient suffering from sprue to that of an individual suffering from Addisonian or pernicious anæmia. The occurrence of gastro-intestinal symptoms in pernicious anæmia has been regarded as significant in this regard and remissions found to occur in both conditions have been the subject of comment. Most stress, however, has perhaps been laid on the blood picture. Nolen in 1918 studied the question and held that it was at times impossible to distinguish sprue from pernicious anæmia. The presence of a high colour index in the blood of patients suffering from sprue is remarkable and has been the most constant point of resemblance to pernicious anæmia. It is of interest here to note that variations frequently occur in the colour index of the blood of patients suffering from pernicious anæmia. Attention has recently been drawn to this by Dr. Knud Faber and Dr. H. C. Gram.[1] They examined the colour index of fifty-four patients with pernicious anæmia and recorded it on admission of the patient to hospital, at the height of remission, just before discharge when the patient was in an unimproved or deteriorated condition and in some instances just before death of the patient in hospital. They found that the colour index was lower during remissions than at any other stage of the disease. A normal colour index was found in only one fourth of the remissions.

The resemblance between sprue and pernicious anæmia has recently been investigated by Dr. C. Elders[2] and Dr. E. J. Wood.[3] The former discusses the relationship of these two conditions from the point of view of their ætiology. He refers to views expressed by himself in 1916 in regard to the nature of sprue. He maintains that it is a deficiency disease. This view has been held by others. Bacterial infections and infections by yeasts have also been looked on as the causative agents. It will be remembered that Ashford maintains that the two factors concerned in the production of sprue are a glandular insufficiency and the superimposition in the digestive tract of a specific organism, the *Monilia psilosis*. Ashford's important work was discussed in THE MEDICAL JOURNAL OF AUSTRALIA, May 12, 1923. Dr. Elders refers to a study made by himself of eleven cases of tropical sprue. In nine instances there was found at times a colour index higher than one. When the colour index was lower than this, he explained it by the occurrence of hæmorrhages from hæmorrhoids. He came to the conclusion that the blood picture could not well be distinguished from that of pernicious anæmia and that the tongue changes could not be distinguished from those seen in this disease. In sprue, as in pernicious anæmia, there is often no hydrochloric acid in the gastric juice and gastro-intestinal disturbances are present in both diseases, though they are more prevalent in sprue. Dr. Elders refers to his criticism of the view that pernicious anæmia is caused by infection or intoxication of exogenic or endogenic origin and that a hæmolytic poison is present. He holds that some features of pernicious anæmia cannot be satisfactorily explained by an intoxication hypothesis and that all its characteristics are easily explicable on a deficiency hypothesis. He states that there is only a slight difference between the two diseases and that if one is a deficiency disease, the other should be so too. In discussing the differences he points out that, though there are gastro-intestinal disorders in both, these may be absent in pernicious anæmia and are more serious in tropical sprue. In the latter condition there is more fermentation in the intestinal canal and acid and gas are commonly produced. The stools have an acid reaction and a higher degree of emaciation is present in sprue. Dr. Elders refers to the unbalanced diet which has been the lot of patients suffering from sprue and to the improvement which has been manifested in these individuals when their dietary has undergone suitable alteration. From this he concludes that sprue is a deficiency disease. He refers to some observations of Ashford on the food taken by patients suffering from sprue, but ignores altogether his work on *Monilia psilosis* in its causative relation to that disease. He states that sprue and pernicious anæmia have so much in common that it is difficult to accept a different ætiology for the two diseases. If they have the same ætiology, he thinks it most probable that pernicious anæmia is, like sprue, a deficiency disease and that as such it should be curable or at least amenable to improvement by well chosen food. This, of course, is not borne out in practice. Dr. Elder's arguments sound very like special pleading. He accepts unproven hypotheses as facts. Moreover, in this paper at any rate, he takes no cognizance of all the

[1] *Archives of Internal Medicine*, December 15, 1924.
[2] *The Lancet*, January 10, 1925.
[3] *The American Journal of the Medical Sciences*, January, 1925.

important work which has been carried out by Hurst and others on pernicious anæmia.

Dr. E. J. Wood in his most interesting article discusses the points of similarity between sprue and pernicious anæmia. Like Dr. Elders, he lays stress on the high colour index found in the blood of patients suffering from the former disease. In every case observed by him the colour index at some stage of the disease has been over one. He refers to the scarcity of observations on the bone marrow in the literature on sprue. Bahr investigated the marrow changes and found no increase in the erythroblastic elements, while in pernicious anæmia characteristic changes were recorded. Bramwell in referring to this work of Bahr held that further observation and corroboration were necessary. Bramwell thought that it was highly probable that in sprue with blood changes so similar to those of pernicious anæmia the same alterations in the bone marrow should be expected. Dr. Wood quotes in some detail the history of a woman who resided for many years in Porto Rico. The findings in her case were very similar to those seen in pernicious anæmia and Dr. Wood adds that he felt that the diagnosis was largely a matter of geography. In the tropics the condition would have been called sprue, out of the tropics it would have been regarded as pernicious anæmia. The suspicion that sprue might be regarded as a type of pernicious anæmia led Dr. Wood to study the occurrence of *Monilia psilosis* in the latter disease. *Monilia psilosis* was found in the fæces of fifteen patients suffering from pernicious anæmia. In two cases only was there any doubt about the diagnosis. The monilia was not recovered in any of forty stools from persons not suffering from pernicious anæmia or sprue. In only one case of pernicious anæmia was any difficulty experienced in growing the monilia from the fæces and this occurred during a remission. In this instance, however, the organism was readily grown from the pyorrhœal gums. During remissions the organisms were found with difficulty or not at all in the fæces. In numerous cases the monilia was obtained from cultures made from the gastric contents. It was suspected that possibly the absence of free hydrochloric acid in the stomach might have been a contributing factor, but this was disproved by finding the yeast in the gastric contents before the occurrence of the usual achylia. Dr. Wood carried out a number of very interesting feeding experiments. He used full-grown guinea pigs. In the case of two animals he used cultures of *Monilia psilosis* grown from the fæces of patients suffering from pernicious anæmia and for another animal he used cultures obtained from an individual suspected of suffering from sprue. In all instances a hæmolytic anæmia was produced and the bone marrow was found to be a deep red colour and to contain an excess of nucleated red cells and an apparent excess of myelocytes. A filtrate of the *Monilia psilosis* which had been grown in dextrose water, was injected into rabbits. After ten days the blood contained nucleated red cells and some of these were of the megaloblastic type. The hæmoglobin value was lowered 15% and the red cells manifested many variations in size and also poikilocytosis. Dr. Wood states that these changes could not be regarded as other than hæmolytic. He holds that the results recorded by him hinge largely on how the work of Ashford is regarded. If the *Monilia psilosis* is accepted as the cause of sprue, the work becomes of great importance. If the monilia is not so regarded, much remains to be done in determining the part which *Monilia psilosis* plays in pernicious anæmia. Dr. Wood states that it is at the present time unimportant whether or not sprue is accepted as a type of pernicious anæmia. Further study and observation must determine the significance of the association of *Monilia psilosis* with pernicious anæmia.

VENOUS PULSATIONS.

THE presence of pulsations in the veins, particularly of the head and neck, may often be noted. In the larger veins, such as the external jugular vein, the pulsation is due to backward pressure from the right side of the heart during systole. Pulsation may also be seen in certain individuals in the veins of other parts of the body. This will be most noticeable if pressure not quite sufficient to obliterate the vein is applied to it from outside. Many observers have discussed this phenomenon and different explanations have been offered. Quincke thought that centripetal pulsation might be due to the propagation of the arterial pulse wave through the capillaries to the veins. He and others described anastomoses between arterioles and venules. It is interesting in this connexion to remember that Boas in discussing capillary pulsation objected to the use of the term capillary pulse as implying active participation of the capillary walls in its production. The same objection might possibly be made to the term venous pulse.

Dr. H. L. White has recently made some observations on centripetal venous pulsations in man.[1] In the first place he gives his reasons for regarding the pulsation as centripetal. His observations were made in an endeavour to determine the extent to which "a pulse could be propagated from the arterial to the venous side of the circulatory bed." The methods used on the subjects were exercise and the application of heat and cold. The subject's exercise consisted in lifting five kilogram weights by extension of the legs. Heat was applied by the partial immersion of the hand in water at 45° C. and cold by partial immersion in water at 5° C.. Some persons manifested no venous pulse under any circumstances. In others the pulsation appeared only after the application of heat and in a third group it was present normally and became accentuated on the application of heat. He explains this by saying that heat caused dilatation of the arterioles and capillaries and cold always contracted these vessels. It was found that cold always abolished the pulsation. He points out that when external pressure is applied the pulsation becomes most evident when the applied pressure equals the diastolic venous pressure.

[1] *Archives of Internal Medicine*, January 15, 1925.

Abstracts from Current Medical Literature.

THERAPEUTICS.

Gold Treatment of Tuberculosis.

L. RICKMANN (*Münchener Medizinische Wochenschrift*, November 14, 1924) states that gold treatment is indicated in tuberculosis when there is a definite lowering in the formation of connective tissue in the foci. It should not be used when the lesion is still active with signs of breaking down tissues and especially when there is much exudation. These patients show a definite reaction with extension of the active processes. The best type of patient for its use is the one suffering from slowly progressing, stationary or retrogressive conditions. Here the gold will stimulate the formation of fibrous tissue and so increase the chance of cure. Laryngeal tuberculosis is best treated both by X-rays and gold. The author has had no experience with the treatment of bone, joint or skin tuberculosis, though many workers state that it gives favourable results.

Pituitary Gland (Posterior Lobe) Extracts.

A. C. KOLLS AND E. M. K. GEILING (*The Journal of Pharmacology and Experimental Therapeutics*, August, 1924) have studied the pharmacology of extracts of the posterior lobe of the pituitary gland. They state that the intravenous injection of Armour's pituitary liquid into animals causes blanching of the skin and visible mucous membranes which is, however, less pronounced in animals anæsthetized with ether. Apnœa with alternating periods of shallow and rapid respiration occurs as a constant phenomenon in the unanæsthetized dog, but when under ether dogs manifest little alteration in respiration. Circulatory changes following the administration of pituitary extracts into sensitive dogs include a rise in the mean blood pressure mainly as the result of an increase in the diastolic pressure due to the increased peripheral resistance, the systolic level playing a subordinate rôle in these changes; a decrease in the pulse pressure; definite slowing of the cardiac rate; a decrease in the minute volume output of the heart and cardiac dilatation as observed with the fluoroscope and on the skiagram. These changes indicate intense peripheral constriction of arterioles and capillaries. Such constriction may be verified by direct observation of the blood vessels of a dog's ear. The bradycardia still occurs when all vagal influence on the heart is neutralized by large doses of atropine sulphate. From this fact it is assumed that pituitary extracts act directly on the myocardium or diminish the flow in the coronary vessels. Oxygen consumption is reduced after the injection of pituitary extract and an increase in the hæmoglobin content of the blood follows immediately, but lasts only for a brief period. An increase in the mean pressure, a rise in diastolic pressure, a diminution of the pulse pressure and cardiac dilatation also occur when the animal is anæsthetized with ether, but to a less noticeable extent.

Oxidized Cod Liver Oil in Rickets.

R. WAGNER AND H. WIMBERGER (*The Lancet*, July 12, 1924) state that no doubt can exist concerning the therapeutic value of cod liver oil in rickets. But it is still debated whether this therapeutic effect depends on its content of vitamin fat-soluble A and can be as readily obtained from other sources of fat-soluble vitamins. McCollum recently showed that two separate fat-soluble vitamins are present in cod liver oil—a growth-promoting and xerophthalmia-preventing principle (vitamin A) on the one hand and a calcium-depositing or anti-rhachitic principle on the other. After subjection to prolonged heating in the presence of oxygen (twelve to twenty hours at 100° C.) cod liver oil retained its property of curing rickets in rats, but had lost all anti-xerophthalmic power. The anti-rhachitic principle is distinctly more resistant to oxidation at 120° C. than the growth-promoting element. The authors treated four infants suffering from rickets with oxidized cod liver oil. The daily dose was ten grammes. The children showed satisfactory healing of the bone lesions at a rate rather slower than with the same dose of a potent, crude, untreated cod liver oil. The growth-promoting potency of the two samples of oil, tested by growth experiments on rats, was found to be in the ratio of about one to twenty. The authors maintain that these observations, though few, lend support to McCollum's view that cod liver oil contains two active organic factors, one anti-rhachitic or calcium-depositing and the other growth-promoting (vitamin A) and that the latter is the more sensitive to oxidation at a high temperature.

Influence of Drugs on the Motility of the Human Stomach.

W. H. DICKSON AND M. J. WILSON (*The Journal of Pharmacology and Experimental Therapeutics*, August, 1924) have attempted to show that the human stomach can be rendered either more or less motile by means of drugs and certain physical influences. Gastric peristalsis can be inhibited wholly or in part by violent exercise, by raising the carbon dioxide content of inspired air and by very large doses of sodium bicarbonate. It is considerably increased by forced breathing and by very large doses of ammonium chloride. The authors concluded also from analysis of the alveolar air that changes in the arterial blood may be responsible for the inhibition or augmentation of the contractions in the above conditions. Gastric inhibition always follows smoking in excess and on occasion it was found to follow the subcutaneous injection of epinephrin. Augmentation always occurs after the administration of coffee, whisky and strychnine in ordinary amounts and after very large doses of magnesium oxide. "Insulin" increases gastric peristalsis to a considerable extent.

Treatment of Pericarditis.

F. KÜLBS AND H. SCHÜRMEYER (*Klinische Wochenschrift*, November 11, 1924) state that pericarditis occurs more frequently than is generally thought, especially as a complication of polyarthritis. Rest in bed until all local symptoms subside is essential. Fluids should be restricted to assist in the absorption of exudate. Cold local applications and the application of leeches are useful for pain and palpitations. Salicylates and quinine should be given and sedatives, such as drugs of the Veronal group, though morphine has generally to be employed. It should be given by mouth or by the rectum. Digitalis should be used in all instances and should not be reserved until signs of cardiac failure supervene. Exploration with a needle is indicated for dyspnœa, cyanosis, intermittent pulse and impending collapse which frequently occurs suddenly. The removal of even one cubic centimetre of fluid may mean the disappearance of these symptoms. The best point at which to puncture is the fifth or sixth left intercostal space just inside or outside the nipple line. If the exudate be purulent the pericardium must be drained.

Iodine Treatment of Goître.

R. ENDER (*Wiener Medizinische Wochenschrift*, November 22, 1924) gives the results of the administration of iodine salts to school children suffering from goître. Out of eighty-four children examined forty-six manifested definite thyreoid enlargement. Twenty-eight were boys and eighteen girls. The children were weighed weekly and the circumference of the neck measured. No ill effects were observed and no loss of weight occurred. On the contrary, all manifested an increase in weight up to two kilograms. After eighteen months' treatment the number of patients with any swelling was reduced to six.

UROLOGY.

"Mercurochrome" by the Mouth.

H. H. YOUNG, W. W. SCOTT AND J. H. HILL (*Journal of Urology*, September, 1924) issue a preliminary report on the use of "Mercurochrome" by the mouth. It was hoped that it might also act as an alimentary tract antiseptic and so help to sterilize the primary focus as well as the kidney in cases of renal infection when an intestinal focus was suspected. It was found that the drug, given in salol-coated pills to prevent absorption from the stomach, could be well tolerated in doses up to three hundred milligrammes given three times a day for a period of seven to twelve days.

The concentration of the dye reaches its maximum in both stools and urine on the fourth day. The germ content of normal fæces was gradually lowered more and more until finally cultures remained sterile. The authors hope in a later report to deal with the action of the drug taken by mouth on patients actually suffering from urinary and alimentary tract infections.

Function of the Vas Deferens After Vasotomy.

W. L. Ross (*Journal of Urology*, August, 1924) prompted by an article published by Brams in November, 1923, in which vasotomy was condemned on account of its liability to be followed by fibrous occlusion of the duct, reports nine instances in which he performed bilateral vasotomy. Opportunity arose only in five of these nine for after-observation of the function of the *vas deferens* by means of massage of the seminal vesicles. In four the massage yielded live, active spermatozoa, while in the remaining patient inactive spermatozoa were found. The essential point in the technique is the making of a clean oblique cut slightly more than half way through the vas. The vas is then made to bend at this point over a support so that the severed lumen is directly in view. This procedure makes it practically impossible to miss the lumen with the cannula. The injection completed, the 5% "Collargol" solution is followed up with about 0.5 cubic centimetre of normal saline solution to drive the "Collargol" remaining in the vas on up into the vesicle. About eight to sixteen cubic centimetres of 5% "Collargol" solution are used on each side. No effort is made to close the incision in the vas itself. Owing to the oblique placing of the cut, the severed edges, when released, fall together automatically. The author points out that although it might be imagined that such a comparatively large cut would afford the maximum opportunity for stricture formation, yet the good results just quoted were obtained. The technique insures efficient injection of the vesicles and helps to prevent the occurrence of peri-ductal infiltration of the tissues of the spermatic cord with the "Collargol."

Resection of the Ductus Deferens.

E. Retterer (*Journal d'Urologie Chirurgicale et Médicale*, September, 1924) publishes his observations on the general state and structure of the testicle two years after resection of the *ductus deferens*. Microscopical examination at this point of time after the operation reveals that the cells of the epithelial layers of the seminiferous tubules pursue their normal evolution, with the exception that there is an absence of the normal liquefaction of the cytoplasm. Moreover, a certain number of nuclei still continue to form the heads of spermatozoa which in the absence of protoplasmic liquefaction remain imprisoned in the epithelial lining. The operation has not affected the circulation of blood, but in the absence of normal functional excitation the epithelium undergoes a simple retardation of nutrition. As regards the inter-tubular tissue, nothing but ordinary connective tissue cells are seen and towards the centre of each lobule this inter-tubular tissue is so poorly developed that the tubules seem to be immediately in contact with each other by means of their basement membranes. There is no reason at all to believe that resection of the *ductus deferens* is followed by degeneration of the epithelium and hypertrophy of the inter-tubular tissue. The division of the testicle into an epithelial gland forming an external secretion and a connective tissue gland forming an internal secretion is a hypothesis founded on gratuitous suppositions. It is refuted by experimentation sufficiently prolonged and controlled by serious histological examination. The results indicate that the epithelium of the tubules manufactures the internal as well as the external secretion.

A New Urinary Antiseptic.

Veader Leonard (*Journal of Urology*, December, 1924) describes "Hexyl Resorcinol," a stable organic substance of known composition, as the most powerful germicide yet discovered in the category of non-toxic substances. It exhibits an increase in bactericidal power of 4,000% over phenol. It is an extremely powerful internal urinary antiseptic and may be administered by mouth in repeated doses for indefinite periods. It exerts, however, little influence, if any, on infections of the renal tissue itself. No true renal antiseptic has yet been found. Prolonged administration of large repeated doses results in no injury to the kidney or irritation of the urinary tract. It retains its bactericidal action in urine of any reaction, a quality which enormously enhances its clinical usefulness. It is excreted unchanged by the kidneys in sufficient concentration to be powerfully bactericidal. Infections confined to the mucous membrane from the renal pelvis downwards can be completely cured with no other treatment than "Hexyl Resorcinol" given by mouth, provided the bacterial count in the urine is not high. When the count is high, the mass action of the antiseptic excreted in the urine is insufficient to complete the disinfection until the count is reduced by local treatment.

Horseshoe Kidney.

N. P. Rathbun (*Journal of Urology*, December, 1924) makes a study of the clinical aspects of horseshoe kidney. According to autopsy and operating table findings the incidence is about one in one thousand. In one out of every six of these some pathological condition of the kidney is present. Horseshoe kidneys are usually found quite by accident in the course of some abdominal operation and less frequently during operations on the urinary tract itself in which some pathological condition but not the anomaly has been diagnosed. With the advent of pyelography it should be possible to make a correct diagnosis in practically every instance. In dealing with an abdominal tumour covering part of the middle line, the possibility of its being a horseshoe kidney should be remembered. This possibility is made more likely if symptoms referable to the urinary tract are present. A symptom suggestive of horseshoe kidney occasionally occurs; this is pain across the abdomen, relieved by lying down and referred from one kidney region to the other. The mass formed by a horseshoe kidney lies as a rule lower than the usual kidney level and the patient may notice the presence of the tumour himself. In the radiogram a kidney shadow lower than normal and very close to the vertebral column is suggestive. In the normal kidney shadow the medial border of the kidney forms an acute angle with the vertebral column at the upper end. The reverse often occurs in horseshoe kidney and in addition the upper pole, less clearly defined than the lower in normal cases, may be quite clearly distinguished. Bilateral pyelography is considered dangerous, but in order that the two pyelograms may be compared one may be taken a few days after the other.

Drugs for Injection into the Vas Deferens.

H. C. Rolnick (*Journal of Urology*, December, 1924) publishes a report on ninety-one vasotomies performed on dogs. He also discusses clinical observations in patients. Various medicaments were employed in different concentrations. At varying intervals afterwards the dogs were killed and the *vasa deferentia* removed in their entire extent. The author determined the state of the lumen of each vas by injecting a 25% solution of sodium iodide and taking radiograms. It was found that in the great majority of instances the recently introduced mercurial antiseptics, "Mercurochrome," "Meroxyl" and "Mercurophen," destroyed the epithelium widely and caused subsequent occlusion of the vas. The destruction of the epithelium was verified by microscopical examination. In one quarter of the cases in which it was used, a 10% solution of "Collargol" led to occlusion of the duct. The safest antiseptic was found to be "Chlorazene" (chloramine-T) which even in a 2% strength caused occlusion in one only out of twenty cases. Clinically it is injected in much weaker concentration (one in one thousand to one in five hundred). The occlusion results from fibrous tissue replacement after widespread destruction of the epithelium, which consists of only one layer of cells. The operative trauma of the vasotomy itself will not cause occlusion unless it is very extensive. Leaving a cannula in the vas for daily irrigation (vasostomy) almost certainly results in occlusion. If it is necessary to repeat the simple vasotomy, it should not be performed until four to six weeks have elapsed and then at a different site.

British Medical Association News.

SCIENTIFIC.

A meeting of the Eye, Ear, Nose and Throat Section of the Queensland Branch of the British Medical Association was held at the B.M.A. Building, Adelaide Street, Brisbane, on December 5, 1924.

Jaw Winking.

Dr. E. O. Marks showed a male patient, aged seven years, who had attended the Hospital for Sick Children on account of a marginal blepharitis. His mother had stated that his right eye seemed to open and shut when he was eating and sometimes when seen from the side appeared to be protruded and withdrawn. This had been noticed since he was very small and had possibly improved to a slight extent. The movement was more noticeable at times than at others and was most noticeable ("something awful") when the boy was hungry. Sometimes but not always the right eyelid was noticed to droop a little.

Dr. Marks pointed out that the child was a normal though a rather delicate looking boy. At times there was a slight ptosis of the right upper lid, otherwise the ocular muscles seemed normal. There appeared to be no weakness in the right *levator palpebræ* muscle, for the lid moved well when the boy looked upwards. He had an unequal hypermetropia, five diopters in the right and 1.5 diopters in the left eye. The vision in the right eye was $^6/_{60}$, with a five diopter lens it was $^6/_{24}$. Vision in the left eye was $^6/_5$. The fundi and the media appeared normal. The defective vision in the right eye was presumably due to an amblyopia resulting from the anisometropia. There was no squint. On opening wide his mouth the patient's right upper lid rose slightly and returned to its former position when the jaw closed. A side to side movement of the jaw elicited this movement of the lid more effectively and it was well shown when he was chewing. The lid became raised as the jaw moved to the opposite side. The amount of movement was variable and was greater when the patient forgot that he was under observation.

Dr. Marks said that the boy was one of those rare curiosities known as jaw winkers. The condition had first been described in 1883 by Marcus Cuvier. Since that time a considerable number of cases had been recorded. In 1895 Sinclair had been able to find records of thirty-two in the literature. Dr. Marks had no idea what the total would be. A large majority of the patients had some degree of ptosis in the winking eye and the majority of them were children. In one instance the ptosis had been present in the non-winking eye. In every patient one eye only had been affected and he had seen no reference to any movement of the lower lid. A patient of Bishop Harman had been thirty-eight years of age and the age of another had been recorded as twenty-seven, so that all did not lose the synkinesis with maturity. In most text-books the condition was described as being due to some error in the connexions of the nerve supply to the various muscles. Dr. Marks thought that this seemed very obvious and really amounted to a somewhat camouflaged confession of ignorance. Bishop Harman in 1903 had studied the nuclear nerve supply of the *orbicularis* muscle, then in dispute, and had investigated the developmental origin of the corresponding muscles in sharks. He had found two layers of muscles, superficial and deep, controlling the movement of the spiracle or first gill and the maxillary cartilage. There was an associated movement between these muscles; when the mouth was open, the gill was open. These two muscles corresponded in man to the facials and the pterygoids. Bishop Harman suggested or rather he stated definitely that human jaw winkers were a survival of this phenomenon, that they were an atavistic anomaly. He considered that the weakened levator muscle indicated by the ptosis rendered noticeable the action of its opponent the *orbicularis*.

Dr. Marks said that this very ingenious and picturesque interpretation presented difficulties which seemed to him to prevent its acceptance. Ptosis was not always present in these cases and when present was just as likely to be the result of the anomalous innovation as to be one of the causes of its inhibition. In the patients whom he had shown, ptosis was present only at times, it was slight and there was no reason to suspect a weakness of the levator action apart from this. Further if the *orbicularis* was responsible for the movement of the lid, the lower lid should manifest the movement as well. It did not, however, do so and no instance of such action on its part had been recorded. It would be expected according to Bishop Harman's views that the phenomenon would often be bilateral and involve other parts of the facial musculature. Records apparently did not reveal this in any instance. There was no evidence at all that the *orbicularis* was responsible for the movement and he thought that those present would agree with him that the movement in his patient was more suggestive of a levator action. In some of the patients reported as manifesting ptosis, the ptosis was not nearly overcome, but the lid was raised higher than its fellow when the jaw movement took place. It was hard to credit that this could be due to the combination of a weakened levator and an action of the *orbicularis*.

As no reference was made in the record to the refractive condition of the patients he presumed that no abnormality had been present. Anisometropia such as that found in his patient was common and its presence was in all probability merely a coincidence. People with a high refractive error in one eye sometimes had a tendency to close that eye to avoid confusion with the better one. It was possible, therefore, that the ptosis present might be due either in part or entirely to the anisometropia. The abnormal movement of the upper lid was not a little suggestive of some anatomical abnormality by which the movement of the temporal muscle might be conveyed mechanically to the orbital fascia and the levator.

Dr. J. Lockhart Gibson said that Dr. E. O. Marks's case of shutter-like movement of one upper lid associated with jaw movements and especially with lateral movements of the lower jaw, was most interesting. He did not remember ever having seen a case of the sort, although he had seen a good many cases of spasmodic movements of the *orbicularis*. He was quite satisfied that the movement in this case was not due to the *orbicularis*. The lower lid was not at all involved. It was impossible to say that the levator was not implicated, especially in the lifting part of the movement, but he thought that fibres of the temporal muscle were the real instigators.

Dr. Alexander MacDonald considered that Dr. Marks's patient would be best treated by suitable glasses. The lens might continue to be dislocated and finally to leave the pupil area.

Dr. George Thomson recommended a spherical lens of ten diopters.

Lesion of Face.

Dr. E. Culpin showed a male patient, aged thirty-five years, married, with three children, a painter, who had been referred by the resident medical officer on account of a swelling just lateral to the right side of the nose and suggestive of lachrymal sac infection. There was a firm almost cystic swelling about the size of a broad bean just below the area of the right lachrymal sac. The swelling had been present for four days. The patient complained of much discharge from the right eye and slight discharge from the right nostril. There was always more or less nasal obstruction on the right side. The tonsils were represented by ragged remnants. Extreme pyorrhœa was present, but the teeth appeared to be sound. There was a definite blue line in the gums and the patient gave a history of plumbism three years previously. In the centre of the palate was an excavated, clean and glazed-looking area about the size of a three-penny piece. Extreme septal deflection to the left side was present. The patient denied having suffered from venereal disease. His arteries were somewhat hardened.

Dr. W. N. Robertson, C.B.E., discussing Dr. Culpin's patient, said that possibly pressure from the badly deflected septum together with some nasal infection was the exciting cause of the condition. He recommended submucous resection of the septum.

DR. J. LOCKHART GIBSON advised incision down to the bone.

DR. H. V. FOXTON recommended the performance of a Wassermann test prior to operation on the septum.

Traumatic Epilepsy.

DR. ALEXANDER MURPHY, M.C., read the history of a patient who suffered from traumatic epilepsy associated with a foreign body, a bullet. Operation had resulted in an apparent recovery though the foreign body had not been removed.

Acute Otitis Media with Involvement of the Mastoid Process.

DR. W. N. ROBERTSON, C.B.E., showed two patients who had suffered from acute *otitis media* with involvement of the mastoid process. The first patient had been seen on August 4, 1924. He had suffered from acute *otitis media* following influenza. The tympanic membrane had been typically fat and boggy. On August 5, 1924, the tympanic membrane had been freely incised in the Alexandra Hospital. The ear had apparently recovered. On September 3, 1924, the patient had suffered from acute earache and the following day Dr. Robertson had discovered a sinus opening into the meatus immediately external to the tympanic membrane. On September 5, 1924, he had operated on the mastoid. The upper half had been quite healthy and the lower half completely disorganized.

The second patient had been sent to him on November 3, 1924, by Dr. Webb. He had suffered from influenza for three weeks and this had been followed by an attack of earache. On examination Dr. Robertson had discovered a sinus external to the tympanic membrane. The tympanic membrane had been congested but not puffy. He had cleaned the ear out for two days and the discharge had ceased. The tympanic membrane had become congested and slight tenderness and swelling had appeared over the mastoid. "Antiphlogistine" treatment had been tried, but with no result. On November 17, 1924, he had operated on the mastoid in the Alexandra Hospital. The upper half of the mastoid process had been healthy and the lower half had consisted of a bag of pus and granulation tissue. This had been cleaned out and treated by the blood clot metnod. The patient had returned to his ship and on November 27, 1924, when the tympanic membrane had been of a good colour.

In discussing these cases Dr. Robertson pointed out that the closing of the sinus had brought about the inflammation in the mastoid, as was often seen with closure of the tympanic membrane. The middle ear had completely recovered in a few days. In the second case by simply cleaning out the diseased tip of the mastoid process he had been able to shorten considerably the period of convalescence, for the inflammation in the tympanum and the antrum had resolved and both areas had been shut off from the diseased area.

Bilateral Microphthalmia.

DR. E. J. MCGUINNESS showed a male patient, aged four and a half years. There was no consanguinity in the parents. The parents' eyes were normal. One sister, aged two and a half years, had no malformation of the eyes. The child's vision was less than $^6/_{60}$ as judged by the "illiterate chart." The child could distinguish objects such as a pencil and watch at a distance of 22.5 centimetres (nine inches). Several congenital anomalies were present. Each eye was microphthalmic. A coloboma was present in each iris. The chorioid and retina existed in both eyes. Right convergent concomitant strabismus and nystagmus were present. Dr. McGuinness pointed out that an unusual feature of the case was the presence of *ectopia lentis*, both lenses being displaced downwards and backwards.

Discussion arose as to treatment by refraction. The general opinion was in favour of correction by glasses of the aphakic area of the pupil owing to the fact that the aphakic area was larger than that in front of the lens.

DR. J. LOCKHART GIBSON thought that the child shown by Dr. McGuinness was affected by micro-cornea more than by microphthalmos. The corneæ, though very small, were clear. No doubt there was irregular corneal astigmatism. The lenses were displaced downwards and backwards but were not tremulous and would probably do no harm. No doubt a high + glass would give useful, though not good, vision through the aphakic part of the pupil in each eye. The existence of coloboma of the chorioid as well as of the iris meant that any rays penetrating through the displaced but clear lenses would fall on the colobomatous part of the fundus. A laryngoscopic mirror proved very useful in examining such patients.

Paralysis of the Right External Rectus Muscle.

DR. GEORGE THOMSON showed a patient who was suffering from paralysis of the right external rectus muscle. The onset had been sudden and there was no ascertainable cause. The patient was an otherwise healthy athlete. The condition was improving and very careful investigation had been carried out in an endeavour to find a cause, but without result.

DR. J. LOCKHART GIBSON said that regarding Dr. George Thomson's case of paralysis of an external rectus in a young abundantly healthy man he was of opinion that in spite of a "negative" history and the absence of a reaction to the Wassermann test, the possibility of its being a manifestation of otherwise latent syphilis should be borne in mind. Recovery without treatment would not exclude syphilis. He told of a similar case seen by him only once in consultation long before the days of the Wassermann reaction. He had advised anti-syphilitic treatment. It was not carried out. Ten years or so later the patient, suffering from locomotor ataxia, had reproached him with failure to seize the opportunity of preventing such a consummation by treatment. He (Dr. Gibson) had not been to blame.

MEDICO-POLITICAL.

THE OBSTETRIC INQUIRY COMMITTEE OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was appointed by the Branch to investigate the whole subject of obstetric practice in Victoria. With the object of obtaining information which might be useful, a *questionnaire* was issued to medical practitioners in Victoria.

The Council of the Victorian Branch has asked us to publish the following epitome of the replies to the several questions.

An Epitome of Replies Received to Questionnaire Issued by Special Obstetric Inquiry Committee.

Question 1.—Do you attend obstetric cases in your practice?—Total number of replies received was 236, of which 208 were from obstetric practitioners and 28 from those who were not (the latter did not answer the remaining questions).

Question 2.—What proportion of your cases are attended:

(1) In hospitals? 67%.
In private houses? 33%.

(2) (*a*) Under the care of unregistered persons?
In 124 practices, nil.
In 41 practices, up to 5%.
In 13 practices, between 5% and 10%.
In 10 practices, between 10% and 25%.
In 5 practices, over 35% (possibly misunderstood the question).
Fifteen replies were unintelligible.

(*b*) Under the care of registered midwives?
(i.) Registered after prescribed course of training, 55%.
(ii.) Recorded without examination before December, 1915, 45%.

(3) Do you consider that your mortality or morbidity rate is influenced by any of the above factors?

21 practitioners were doubtful or gave no answer.
82 practitioners considered these factors did not influence.
105 practitioners considered these factors did influence.

Question 3.—Do you prefer to attend patients in hospitals or in their homes?

194 practitioners preferred attending patients in hospitals.
8 practitioners preferred attending patients in their own homes.
6 practitioners stated their preference depended upon the type of home and standard of hospital available.

Question 4.—Do you have any difficulty in obtaining efficient maternity nurses?

100 practitioners have had difficulty.
101 practitioners have had no difficulty.
7 practitioners did not answer.

In the event of a patient going to a hospital, is there any difficulty in obtaining domestic help in her own home during her absence?

160 practitioners have difficulty.
36 practitioners have no difficulty.
12 practitioners did not answer.

Question 5.—Can you give any idea of the proportion of cases in your district attended solely by midwives?—Only 116 definite answers—

12 practitioners, nil.
43 practitioners, under 5%.
25 practitioners, between 5% and 10%.
25 practitioners, between 10% and 30%.
11 practitioners, over 30%, highest 60% (probably question misunderstood).

Question 6.—Would you have any objection to making notifiable to the Health Commission all maternal deaths occurring during the period embracing the last three months of pregnancy and the first three months after delivery?

3 practitioners did not reply.
4 practitioners would have objection.
201 practitioners would have no objection.

Question 7.—What ante-natal care is it possible for a woman to receive in your district if she has not engaged a doctor?

Baby health centres mentioned by 25 practitioners; public hospitals mentioned by 20 practitioners; bush nurses mentioned by 8 practitioners; district nurses mentioned by 3 practitioners; private hospitals mentioned by 4 practitioners. All others replied to the effect that there were no ante-natal facilities or that they were not cognizant of any.

Are there any suitable hospitals in your district to which a patient can be transferred for obstetrical treatment?—Twenty-two practitioners (practically all country) had either no hospital or an unsatisfactory hospital. Many of these made use of hospitals some miles distant. All other answers were in affirmative.

Question 8.—Are you satisfied with the asepsis and practical knowledge of the nurses?

98 practitioners were satisfied.
36 practitioners were dissatisfied.
72 practitioners were satisfied with hospital trained nurses, but not with "Gamps."

If not, can you suggest any improvement in the present methods of their training?—Sixty-five made suggestions as to improvements. Some suggested more practical work, others more theory and practice of asepsis and antisepsis. De-registration and prohibition of private training schools was asked for by several, whereas some country members asked that private training be recognized in country centres at least. Two suggested a college of nursing with a diploma or degree, thus abolishing apprenticeship system. (Several singular suggestions of value were made, but are not published herewith.)

Question 9.—Have you any suggestions to make as to an improvement in the present method of training of students?

Only 95 made suggestions. Two thought the present method was adequate. All the comments concerned the practical (clinical) work. A few suggested six months' residence at the Women's Hospital as a minimum, whereas several thought three months should be required. Others expressed it on the basis of a minimum number of cases—from twenty to fifty. Not many discriminated between "*interne*," "*externe*" and out patient ante-natal practice. In the replies of those that did so, ante-natal work was emphasized in 16, "*externe*" work in 11, after treatment and post-natal in 9.

As regards the nature of the "*interne*" work it was frequently implied and sometimes stated that students should be given more responsibility in the conduct of abnormal cases. Practice in the application of forceps was suggested by many. As regards the organization of the teaching staff and the clinical material to effect these reforms there were fewer suggestions.

Twelve replies contained a suggestion that there should be a full-time director of obstetrical studies (especially clinical) either in the form of a university professorship or a hospital mastership (as at Rotunda). Six stated that more metropolitan obstetrical clinics should be established. Divorcement of the teaching and practice of obstetrics and gynæcology was recommended by two, whereas two others suggested a closer *liaison*.

Seven recommended the system of private apprenticeship of students to selected obstetric practitioners (before and after graduation) apparently (although not specifically stated) in addition to practical work at public hospitals. (Several singular suggestions of value were made, but are not published herewith.)

Question 10.—Would you suggest any alteration in the present allocation of the Maternity Bonus?

24 practitioners gave no answer.
55 practitioners preferred no alteration in present allocation.
127 practitioners preferred an alteration in present allocation.
2 practitioners thought an alteration was desirable in the city, but not in the country.
34 practitioners suggested a class distinction in its allotment (that is income limit).
45 practitioners claimed that it should be earmarked for medical and nursing expenses. This according to some was to be insured by making bonus payable only on certification that confinement was conducted in a hospital.
5 practitioners suggested payment of bonus prior to confinement conditionally upon the notification of pregnancy.
50 practitioners' replies contained suggestions that the mother should no longer be the payee, but the money funded to provide maternity hospitals, wards or beds (of public, private or intermediate character) with ante-natal and post-natal clinics and infant welfare centres.
3 practitioners suggested that a part of the money should be utilized in obstetrical education and research.

Question 11.—Have you any knowledge of instances in which the Regulations under the *Midwives' Act, 1915*, have been abused or otherwise rendered ineffective?

46 answered in the affirmative, considerably more than half of these being country practitioners.
19 specified the attendance of unregistered persons.
3 mentioned cases in which registered midwives took several patients into their own homes, which were not registered hospitals.

In what direction, if any, could they be improved?—The view was expressed by most that the regulations, good as they may be, were a dead letter owing to ineffective administration. Nearly all thought that practically no steps were taken to enforce the regulations by effective supervision, inspection and punishment for breaches. Practically the only suggested improvement in the text of the regulations was the introduction of two classes of registered midwives (*a*) after prescribed course of training and examination, (*b*) recorded. Class (*b*) not to be allowed to take cases except with a doctor.

Question 12.—For how long do you regard it as being necessary to visit a patient after a confinement?

202 definite answers, with an average of 12 days.
12 mentioned subsequent visits for purpose of vaginal examination.

Question 13.—Are you satisfied with the amount of fee usually paid for your midwifery work?

89 were unreservedly satisfied.
107 were unreservedly dissatisfied.
9 were satisfied only if no complications or if patient is confined in hospital.
3 gave no answer.

Is ante-natal attendance included in the fee?

45 said ante-natal attendance was not included in fee.
156 said ante-natal attendance was included in fee.
4 said ante-natal attendance sometimes included.

Question 14.—What proportion of the mothers in your practice breast-feed their babies and to what extent?

Twenty-two gave no answer, 186 practically all thought that except in rare cases all mothers breast-fed the child whilst the obstetrician was in attendance.

As regards subsequent feeding, varying percentages of the mothers (25% to 100%) breast-fed their babies for varying periods (from two to ten months).

In some statements cases of mixed feeding were included, but in most the implication was that the breast-feeding was not supplemented.

As a very rough index it may be said that about 60% of mothers entirely breast-feed their babies for periods of six months or longer.

Medical Societies.

THE ALFRED HOSPITAL CLINICAL SOCIETY.

A MEETING OF THE ALFRED HOSPITAL CLINICAL SOCIETY was held on November 25, 1924, at the Alfred Hospital, Melbourne, MR. FAY MACLURE, O.B.E., the President, in the chair.

Lesion of the Finger.

DR. JOSEPH LOVE showed a girl, aged eighteen years, who had noticed a swelling over the dorsal aspect of the terminal phalanx of the right thumb for the previous six months. During the preceding eight days the swelling had increased and had become tender. An incision had been made into the swelling in the casualty department, but no pus had escaped. On examination the interphalangeal joint was found to be very lax so that the bones could be freely moved in all directions over each other. This movement did not cause pain. Creaking or crepitus was not obtained. Dr. L[illegible] showed a skiagram which did not reveal any abnormality of the bones. The patient's serum had not reacted to the Wassermann test. Dr. Love asked whether this condition involved the joint cavity or only the ligaments. What was the condition? What treatment should be carried out?

DR. F. K. NORRIS said that he regarded the condition as of tuberculous origin, an opinion in which Dr. Jones concurred.

MR. BALCOMBE QUICK, O.B.E., suggested that it was a "butcher's" wart and thought that a section should be cut.

Infiltration of the Urethra.

DR. R. FOWLER, O.B.E., showed a woman with a condition of the urethra resembling a soft infiltration or early stricture in the male. The cause was not evident, as gonococci had not been isolated. The patient's serum had reacted to the Wassermann test.

Spastic Quadriplegia.

MR. H. C. COLVILLE showed a boy, aged eight years, who from birth had suffered from a condition of spastic quadriplegia. The mental development was moderately good. Voluntary control of the limbs was absent, its place being taken by convulsive and athetoid movements. On October 16 Mr. Colville had performed sympathetic ramisection on the right upper limb following Royle's technique. Next day the limb had been flushed and definitely less spastic than its fellow. It had offered much less resistance than before to passive movements. Since then there had been no appreciable change in the condition of the limb. Mr. Colville hoped that education would be facilitated by the relief of spasticity already obtained and requested that others should state their opinions as to whether or not the other limbs should be similarly treated.

DR. J. F. MACKEDDIE said that he was impressed by the distinctly encouraging result and advised Mr. Colville to continue with the treatment of the other limbs.

Wound of Brachial Artery.

MR. HUGH TRUMBLE, M.C., showed a man who, whilst attempting to adjust a belt on a pulley, had had his arm caught by it and had sustained a gash on the inner aspect of the arm just above the elbow. The brachial artery had been severed. The man's mates had tied a bandage tightly around the arm and the bandage had not been removed until admission to hospital five hours later. Blood had been transfused, the wound had been cleaned under block anæsthesia, the brachial artery had been tied and the median nerve, which was severed, sutured. Next day the arm and hand had recovered their warmth, but there had been no sensation over the forearm excepting about the radial border down to the base of the thumb and no voluntary contraction of forearm or hand muscles could be observed. About a week later the tips of the fingers had begun to dry and shrivel and the gangrenous process had spread until involving the greater part of the hand. The area of sensibility had remained the same. No evidence of nerve regeneration had been obtained after one month. Mr. Trumble asked whether anyone could inform him as to the amount of regeneration to be expected.

MR. FAY MACLURE, O.B.E., referred to a case in which to facilitate an operation on the elbow, a broad elastic band tourniquet had been applied to the upper part of the arm and left on for about one and a half hours. On recovery from the anæsthetic the girl had not been able to move her hand and not until six weeks later had she shown signs of recovery. He believed that she would recover completely. Mr. Maclure had not seen gangrene of the upper limb following an arterial injury, though this accident might be followed by a limitation of activity in the limb resembling intermittent claudication.

DR. J. F. MACKEDDIE said that he was interested as to how far the nervous injuries were responsible for the gangrene.

DR. M. D. SILBERBERG thought that in the presence of both nerve and arterial damage the capillaries might pass into a state of spasm and that this might explain the gangrene.

Hand Dystrophies.

DR. J. F. MACKEDDIE showed two patients suffering from hand dystrophies. In one the condition was due to cervical rib and in the other it was of central origin. In the first patient the cervical rib had been removed one month previously by Mr. Maclure and since then considerable improvement had taken place.

Dr. Mackeddie also gave a demonstration of the use of "Lipiodol" in spinal tumour localization.

Syphilitic Mediastinitis.

Dr. Walter Summons, O.B.E., showed a patient suffering from syphilitic mediastinitis. The patient had been shown first at a clinical meeting some months previously.

Under anti-syphilitic treatment definite clinical and symptomatic improvement had taken place and a series of X-ray photographs demonstrated clearly, when compared with those originally taken, the good results of treatment.

Congenital Heart Disease.

Dr. F. Kingsley Norris showed a female infant, aged five months, who had had attacks of cyanosis and dyspnœa every few weeks since birth. There were no detectable heart murmurs. The red blood corpuscles numbered 7,480,000 per cubic millimetre. The reaction to the Wassermann test had been "partial." The family history showed that one sister had died at two months from congenital heart disease with a septal defect associated with a systolic bruit. Another sister had died at two and a half years following a severe convulsion. A specimen demonstrated at the meeting showed absence of interauricular septum, one vessel straddling both sides of the heart, developing into an aorta and giving off small pulmonary vessels. The Wassermann test in this case had also yielded a "partial" reaction. One brother aged three years was apparently well.

Dr. Norris's second patient was a boy, aged two years, who had been intensely cyanosed since birth with dyspnœa at times after food. During the previous twelve months he had survived a severe attack of pertussis complicated by broncho-pneumonia. His general condition at the time of demonstration was very good. The red blood corpuscles numbered 8,300,000 per cubic millimetre. The heart sounds were normal.

Dr. M. D. Silberberg said that not all these patients were syphilitic. He quoted the history of a girl first seen at age of eight years who developed well up to sixteen years before showing any symptoms of cardiac distress.

Dr. Robert Fowler mentioned the history of a woman aged twenty-two who had been in labour and very cyanosed and had died from heroin poisoning. *Post mortem* examination had revealed a large *ductus arteriosus*.

Dr. Spalding Laurie said that the prognosis in these patients was very indefinite and quoted instances of patients who carried on comfortably to adult life. In the patient shown by Dr. Norris he thought the prognosis was bad.

A meeting of the Alfred Hospital Clinical Society was held on February 24, 1925, at the Alfred Hospital, Mr. Fay Maclure, O.B.E., the President, in the chair.

Squamous-Celled Carcinoma Arising in an Old Tuberculous Sinus.

Mr. A. J. Trinca showed a man, aged thirty-two, who had had several operations on a tuberculous kidney, which had left him with a tuberculous sinus. During the last few months a fungating ulcerous mass had grown round the sinus in the skin. The man had been admitted on account of several severe hæmorrhages from the mass. a fungating tumour seven and a half to ten centimetres (three to four inches) in diameter was present in the right costo-vertebral angle with areas of pale œdematous granulations perforated by sinuses and exuberant carcinomatous tissue. Tubercle bacilli had been found in great numbers and a section revealed active squamous-celled carcinoma.

Mr. H. Trumble, M.C., suggested that the growth should be treated by diathermy.

Mr. Fay Maclure agreed, but thought that X-rays should also be used.

Compound Ganglion of Hand and Wrist.

Mr. Trinca's second patient was a woman, aged thirty-five years, who complained of a soft, fluctuant swelling over the volar aspect of the right of wrist, palm and thumb which had developed during the previous two years. It had commenced during the puerperium. The examination disclosed the fact that the process involved the flexor tendon synovial sheaths of the thumb, wrist and palm. Melon seed bodies could be felt. Fluid aspirated was straw coloured and contained polymorphonuclear cells only. Mr. Trinca proposed to aspirate the fluid contents and to inject "Acriflavine."

Otitis Media.

Mr. Bryan Foster showed a man, aged thirty-four years. In November, 1924, earache had started suddenly and had continued since. Pain in the neck had commenced two weeks previously and a swelling had appeared below the mastoid process. The pain and swelling had increased until he could not move his head. There had been no previous ear trouble and no discharge from the external meatus. On examination a Bezold's abscess had been present. The tympanic membrane had been injected, but not perforated or bulging. Hearing had been diminished. The temperature and pulse had been raised. Operation had shown that the mastoid process was perforated near its tip.

Dr. Foster remarked on the unusual absence of perforation and surmised that drainage must have taken place along the Eustachian tube. Bezold's abscess was also somewhat of a rarity.

Mr. Fay Maclure recalled a case of cavernous sinus thrombosis in which an abscess had occurred over the fronto-parietal suture near the vertex. He thought that possibly the unusual extension might be ascribed to a sealing off of bone cells by inflammatory products.

Carcinoma of the Rectum.

Dr. W. J. Saxton showed for Mr. Maclure a man, aged thirty-six years, who had been operated on by Mr. Maclure for carcinoma of the rectum. On October 22, 1924, a laparotomy had revealed that there was no gross involvement of glands. At a further operation on November 1, 1924, the growth had been removed from the perineum and the bowel above had been mobilized and brought through the *sphincter ani externus* which had been isolated. The growth which was low in the rectum, proved to be a columnar cell carcinoma.

The man stated that he could control the bowel action fairly well. A finger in the anus demonstrated that there was quite good sphincteric action.

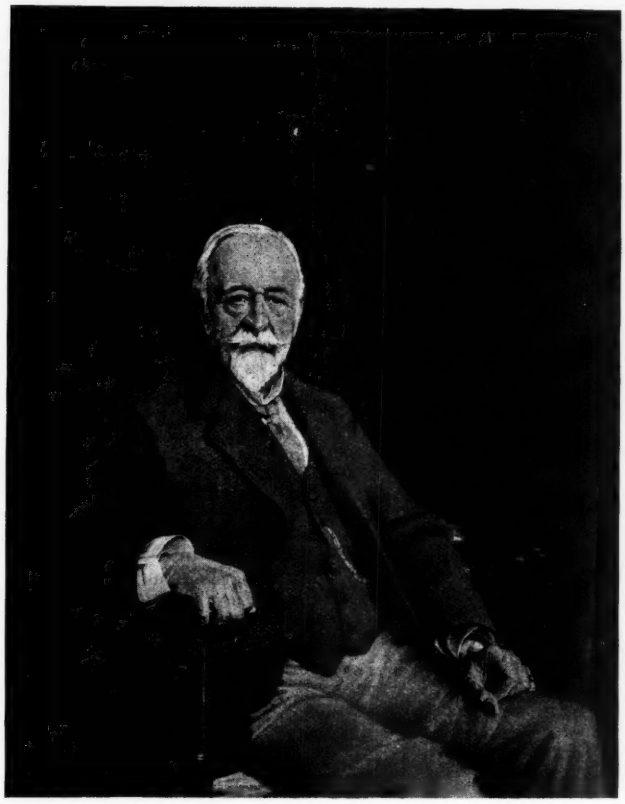
Mr. Hugh Trumble showed a man, aged sixty-one years, who had been admitted in April, 1924, with intestinal obstruction, the cause of which was undiagnosed. Laparotomy had disclosed a tumour in the rectum just below the promontory. A colostomy of the descending colon through the right rectus muscle had been performed. In May the tumour had been resected from the perineum, portion of the sacrum being removed. The lower five centimetres (two inches) of the rectum had been left and the bowel above the tumour had been united to this portion. The wound had suppurated, leaving a somewhat narrowed lumen at the site of union. By giving himself an enema through the colostomy stoma the patient had been able to insure that the colon would empty itself each morning and not again during the twenty-four hours. In January, 1925, the colostomy had been closed. At the time of demonstration the patient had no trouble of any sort, he was putting on weight and was back at his occupation as a school teacher. The bowels acted normally each day with no other medicine than fifteen cubic centimetres (four fluid drachms) of paraffin daily.

Obituary.

THOMAS CLIFFORD ALLBUTT.

Professor Sir Thomas Clifford Allbutt, K.C.B., F.R.S., is no longer. He lived an example to his contemporaries and to those who follow him. He will be remembered for his general learning, for his achievements in medicine, for his power to convey in pure, elegant English valuable messages derived from his philosophical mind, for his beneficent influence on medicine of his day.

Thomas Clifford Allbutt was born in 1836 in Yorkshire. He was educated in the same county under Archdeacon Hey. At an early age his teachers and friends endeavoured to awaken in him a strong leaning towards music, but the appeal did not reach his soul and thus missed the mark. Later he travelled in Italy because the ecclesiastic dignitaries who exercised a strong influence on his home, were under the spell of the pre-Raphaelite movement and considered that young Allbutt must devote himself to art. But he had no gift for expression in this direction. At about the age of twenty he became aware of a natural tendency toward science. It has been said that the reading of Comte's "*Philosophie Positive*" awakened his latent interest in philosophy and scientific research and determined him to select the profession of medicine as a calling. He read for the science tripos and graduated first class in 1859 with distinction in chemistry and geology. He obtained his arts degree in 1860 and a few years later a degree in medicine. In 1868 he gained the degree of doctor of medicine. His early work was carried out at Addenbrooke's Hospital, Cambridge. He then moved to London and worked at Saint George's Hospital for a short time, but he disliked the metropolis and chose Leeds as a more congenial place for medical practice. He was appointed physician to the Leeds Fever Hospital and on several occasions he was in sole charge of the institution during epidemics of typhus fever and variola. He attracted attention and opposition by the introduction of certain hygienic expedients in this hospital. He had the windows of the wards opened and kept open by nails driven into the sashes. That the mortality was reduced by improved ventilation of the sick room is unquestioned. His paper on the origin and rationale of the hygienic treatment of typhus and small pox was read with interest and some scepticism by the authorities in sanitary science of the day. Allbutt was not content with the results or with the attempt to improve the chances of those stricken with these diseases; he was determined to make a bold bid for their prevention. He promoted a company for the erection of model workmen's houses in Leeds in the hope that both diseases would disappear if the masses lived in hygienic environments. He instituted the Leeds Sanitary Association with the same object. This early work was of the greatest importance in inducing the public health officials to recognize their functions and to exercise an intelligent interest in the accumulation of scientific knowledge. From this time until 1892, when he was appointed Regius Professor of Physic at the University of Cambridge his career was marked by a succession of triumphs. He was a pioneer and his master mind, teeming with ingenious argument, compelled his contemporaries to realize the advantage of the practical application of scientific principles to hygienic problems. He had studied under Trousseau at l'Hôtel Dieu and also under Bazin at Saint Louis. From Duchenne he had acquired an interest in neurology and at this great clinician's hospital he had laid the foundation of an extensive neurological knowledge.



It would occupy more space than we have at our disposal to trace the long and honourable career of Thomas Clifford Allbutt from the time when he served at the Leeds Fever Hospital until he occupied the President's chair of the British Medical Association from 1915 to 1920. Nor is it necessary, for his name is a household word in the world of medicine. Honorary degrees were showered on him. He was an honorary Doctor of Science of the University of Oxford and a Fellow of the Royal Society. He held many important positions in hospitals. His versatility is evidenced by the facts that he was appointed a Commissioner in Lunacy in 1889, a member of the Council of the Royal Society in 1896 and Vice-President in 1914, a member of the committee of the Home Office on trade diseases and a member of the Committee on National Research. He is known to every medical student as the editor of Allbutt and Rolleston's "System of Medicine" (1896 to 1907). He was a prolific writer, but all he wrote was worthy of close study. His contributions on diseases of the central nervous system and on the heart were all masterpieces. In 1909 he delivered the Fitzpatrick Lecture and selected the subject of Greek Medicine in Rome. He invented the short clinical thermometer, an achievement which contributed to the universal employment of this instrument.

Thomas Clifford Allbutt leaves a record of half a century of professional life, as one of the greatest thinkers and teachers of his time. His personal charm linked with his extraordinary knowledge of life and living things remain in the memory of all who came under his influence. The world is a better place because of that influence.

EUSTACE JULIAN KEOGH.

A LARGE circle of friends and many grateful patients, particularly among the poor of South Yarra, mourn the loss of Dr. Eustace Julian Keogh whose death was recorded in our issue of March 7, 1925.

A Melbourne boy, Eustace Julian Keogh was educated at the Alma Road Grammar School and afterwards at the Christian Brothers' School, St. Kilda. From here he matriculated and went to Edinburgh University to study medicine. At Edinburgh he was one of a large Australian group of students which included Sydney Jamieson, A. L. Kerr, P. J. Kenna and Roland Pope, of Sydney, Barnett and Somerville, of New Zealand, Gibson and Scott, of

Tasmania, Harrold, of South Australia, Marwood, Bryant and Fetherston, of Melbourne. He took part in all the sports and was always ready to give and take a knock in the very best spirit. He graduated as bachelor of medicine and master of surgery in 1888.

On his return to Australia Keogh started practice in South Yarra and continued to reside until his death within a few yards of his original location. When a young man he joined the staff of Saint Vincent's Hospital as assistant physician and was soon afterwards appointed indoor physician, being a colleague of Dr. David Grant. He resigned this position in 1908 because he felt that he could not conscientiously give the time required for the performance of the duties attached to it, his private practice had grown to such an extent. A man of quiet disposition, he was determined, almost brusque in his manner, always holding the highest ideals and having the truest conception of his duties as a medical man to those under his care. In his younger days he took much interest in public and municipal affairs and once contested a seat in the local council.

By the death of Eustace Julian Keogh Victoria loses one of the best type of general practitioner. In spite of a very busy practice he found time to devote a great deal of his energy to the poor of the district, by whom he will be greatly missed. He leaves a wife and ten children.

Correspondence.

POSTURAL TONUS.

SIR: Professor Mills's article on "Some Effects of Disturbance of Physiology of Movements of Gastro-Intestinal Tube" which appeared in your issue of February 7 last, would rather make it appear that the question of postural tonus in visceral and somatic muscular systems had been definitely settled by the recent experiments of the late Professor Hunter and Dr. Royle.

Without going into the actual results of these researches which all agree are of very great value, I would like to point out that the experiences of several Melbourne surgeons in the treatment of spastic conditions by Dr. Royle's method has led them to express opinions quite unfavourable to the procedure.

At the December meeting of the Section of Psychiatry and Neurology, Dr. Sewell read a paper entitled "The Basis of Spasticity" in which he traversed the anatomical and physiological bases of spastic conditions.

This was followed by a discussion in which several surgeons took part. Each of these gentlemen related how, stimulated by Dr. Royle's work, he had operated upon several cases of spasticity after carefully selecting same; Dr. Royle's methods were followed thoroughly, but in no case had the result been anything like what has been claimed.

Some of the cases were undoubtedly less rigid for a period following the operation, but the rigidity gradually returned and the patients were no better. In one case the surgeon thought the improvement which was slight, might remain.

At the Caulfield Repatriation Hospital this operation has been tried, but is now looked upon with disfavour and not performed, although one of the surgeons is (against his own judgement) about to try another case at the urgent request of myself and the patient. The above statements are not my opinion, but are quoted to show that in Melbourne at least surgeons are not impressed with the sympathetic ramisectomy for spastic conditions.

Further it seems that Professor Mills has involved himself in what to me are inconsistencies. He affirms that the sympathetic controls the postural tonus of the bowel so that when the sympathetic is stimulated as by adrenalin or when it is released from higher control as in a transverse lesion of the cord, there is lack of tone in the gut, that is, distension with constipation; on the other hand there is a great increase of postural tonus in the muscles of the limbs and further that when the sympathetic is cut and its influence thereby removed, the reverse phenomena take place—a resumption of tone and activity in the bowel with a lessening of tone in the somatic muscles. There appears to be something contradictory in these conceptions and the experience of surgeons in this city would apparently support my contention.

Again Professor Mills states that in conditions such as sepsis and rickets, "the distension is due to diminution of plastic tonus, the effect of toxæmia upon the sympathetic; the distension of rickets expresses the lowered plastic tonus of the sympathetic." The above quotation is rather confusing to me. What is the effect of poison upon the sympathetic? Does it irritate or does it depress the sympathetic activity? If the former, then distension might occur; if the latter (according to preceding statements), there should be increased activity of the bowel.

It is, of course, conceivable that toxins may either heighten or depress the activity of nervous structures; one toxin may do the former, another may do the latter or either may do both at different stages, but there is nothing to indicate in Professor Mills's address what he really means by the expression "lowered plastic tonus of the sympathetic." Does he mean the condition of the nervous system or the resultant condition in the muscle systems supplied by the nerve elements?

In conclusion, sir, may I submit that the problem of postural tonus and spasticity is not yet solved and that evidently a great deal of patient research will have to be undertaken before we can deal with the problems involved in any simple manner.

Yours, etc.,

PAUL G. DANE.

61, Collins Street, Melbourne,
March 10, 1925.

COLLES'S FRACTURE.

SIR: Allow me to congratulate Dr. Teece upon his very able discussion of Colles's fracture.

In this injury my results have invariably been splendid, the mode of reduction having been the obvious one described in the article.

I have often wondered why the text-books make such a fuss about Colles's fracture, which to my thinking is a mere bagatelle compared to its neighbour—a break of both bones about the middle of the forearm. Yet the latter is usually dismissed with scant notice.

In treating this lesion I have never been able to avoid pronounced angular deformity as a sequel; my escapes from litigation have appeared to me miraculous. I have been tempted to use plaster of Paris dressings, but have been deterred by the dictum of St. Thomas's Hospital that the forearm is the one region of the limbs in which a rigid dressing is inapplicable.

I would be very pleased if Dr. Teece can instruct me how to secure as good a result in one fracture as in the other.

Yours, etc.,

H. LISTER.

Cobargo, New South Wales,
March 4, 1925.

NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

SIR: Many of the country members of the New South Wales Branch of the British Medical Association feel that they would like to have direct representation on the Council.

They have no fault to find with the Council as at present constituted and quite realize how much the Council has done in the interests of medical men in the country.

At the same time occasions must arise in the deliberations of the Council when a direct representative from the country men would greatly help the Council when discussing affairs particularly affecting country interests.

In the past the great drawback to direct representation has been the difficulty in securing any medical man from the country who could spare the time to attend the meetings of the Council.

The Northern District Medical Association is fortunate in having a well-known medical man, Dr. R. M. Kinross, of Inverell, who is willing and able to spare such time.

The members of the Northern District Association at the annual general meeting on January 28 unanimously resolved to nominate Dr. Kinross as a candidate for the forthcoming election of members on the Council and trust his election may be secured by the support of all country members of the British Medical Association.

Yours, etc.,

A. G. BRYDON,
President, Northern District Medical Association.
E. B. FITZPATRICK,
Honorary Secretary.

Pialba.

INFLUENZA.

SIR: Apparently influenza will be among us in a few weeks and I should like to draw attention to one very important way of preventing it. The *habitat* of the influenza microorganism is essentially in the respiratory passages, the nose and throat.

In ordinary conversation the fine spray from the mouth may be carried two or three feet. With a cough or a sneeze the microorganisms are dislodged and may be carried for ten or fourteen feet and they may float about in the air for three or four hours before falling to the ground.

The duration of their capability of infection depends on: (i.) Their age and vitality, (ii.) the temperature of the air, (iii.) the moisture of the air, (iv.) the ventilation of the room (purity of the air). Below 70° F. they would not thrive; on an ordinary cold winter's day they would possibly be harmless within half an hour.

Thus influenza is a disease which is transmitted within narrow limits of time and space direct from the sufferer to the susceptible. One sneeze from an infected person would permeate and pollute the air of a room fourteen feet long. An individual not breathing through his nostrils or a susceptible individual entering this room within half an hour would most likely become infected.

Prevention is easy—like the well-known Bible story, it is possibly too easy—and depends on the patient. When about to sneeze or cough, let the patient hold a pocket handkerchief in front of the mouth and nostrils. Should this be impracticable, then merely use the hand which could be cleansed later or even cough and sneeze towards the ground. In a word conform to the manners of ordinary society. There are legal penalties for spitting, but there is no penalty for the more deadly unguarded sneeze or hacking cough.

We have all seen the vigorous sneezer or the gentleman with the tickle in his throat. They usually seek warm, unventilated rooms and keep the windows shut, ideal conditions for the bacillus.

Let the healthy attend to the general health—avoid stuffy rooms, breath through the nostrils, healthy nostrils within reasonable limits will protect, attend to the teeth, a septic mouth increases the risk of pneumonia and its virulence.

Yours, etc.,

G. L. L. LAWSON, M.R.C.P. (Edin.), D.P.H.

Rooty Hill,
March 7, 1925.

Naval and Military.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Nos. 12, 15, 18 of February 5, 12, 26, 1925:

AUSTRALIAN MILITARY FORCES.

Australian Army Medical Corps (Citizen Forces).

The resignation of Major-General Sir N. R. Howse, V.C., K. C. B., K.C.M.G., of his appointment as Director-General of Medical Services, Army Headquarters (services not wholly employed), is accepted, 16th January, 1925, and he is transferred to the Unattached List, 3rd Military, District, 17th January, 1925.

First Military District.

Australian Army Medical Corps.

The provisional ranks of Captains K. B. Fraser and K. J. G. Wilson are confirmed.

Reserve of Officers.

Major S. H. Seccombe is placed upon the Retired List with the honorary rank of Lieutenant-Colonel and with permission to wear the prescribed uniform, 15th January, 1925.

Australian Army Medical Corps Reserve.

Honorary Lieutenant P. M. Coughlin is retired, under the provisions of Australian Military Regulation 152 (1), 13th January, 1925.

Second Military District.

Australian Army Medical Corps.

Captain R. J. Silverton is transferred to the Reserve of Officers, 1st February, 1925.

Unattached List.

Lieutenant A. E. Heath is transferred to the Reserve of Officers, 16th February, 1925.

Reserve of Officers.

Major A. E. Mills is placed upon the Retired List with permission to retain his rank and wear the prescribed uniform, 13th February, 1925.

AWARD OF THE COLONIAL AUXILIARY FORCES' OFFICERS' DECORATION.

Unattached List.

Lieutenant-Colonel J. C. Storey, O.B.E.

Third Military District.

Australian Army Medical Corps.

Captain H. S. Jacobs is transferred from the Unattached List, 5th December, 1924.

To be Captain (provisionally).—Honorary Lieutenant C. E. V. Sutherland, from the Australian Army Medical Corps Reserve, 1st February, 1925.

Australian Army Medical Corps Reserve.

Honorary Captain A. J. J. Triado is transferred from the the Australian Army Medical Corps Reserve, 5th Military District, 20th January, 1925.

Fifth Military District.

Australian Army Medical Corps Reserve.

Honorary Captain A. J. J. Triado is transferred to the Australian Army Medical Corps Reserve, 3rd Military District, 20th January, 1925.

Sixth Military District.

Australian Army Medical Corps.

Captain H. J. Orr is appointed from the Reserve of Officers, 1st January, 1925.—(Ex. Min. No. 53.).

Major H. Z. Stephens is transferred to the Unattached List, 1st December, 1924. (In lieu of notice which appeared in *Commonwealth Gazette*, No. 1, of 8th January, 1925, page 13.)

Post-Graduate Work.

POST-GRADUATE COURSE IN OBSTETRICS.

THE MELBOURNE PERMANENT COMMITTEE FOR POST-GRADUATE WORK is arranging a winter course of lectures in obstetrics. The lectures will probably take place in June and July on Tuesday evenings at 8.30 p.m. at the B.M.A. Building, East Melbourne. It is hoped that some clinical work may be arranged in conjunction with the lectures. Further details will be announced at a later date.

Proceedings of the Australian Medical Boards.

QUEENSLAND.

THE undermentioned have been registered under the provisions of the *Medical Act of 1867* as duly qualified medical practitioners:

Arrata, Joseph Andrew, M.B., 1922 (Univ. Sydney), Red Hill, Brisbane.
Brown, James, M.D., 1924 (Univ. Edinburgh), Toowoomba.
Drew, Thomas Mitchell, M.B., B.S., 1901 (Univ. Melbourne), Piabla.
Finlay, Cuthbert Clive, M.B., 1923 (Univ. Sydney), Goondiwindi.
Hartridge, Oliver Keith, M.B., B.S., 1912 (Univ. Melbourne), Roma.
Hewitt, George Henry, M.B., 1923 (Univ. Sydney), Mount Morgan.
Hollingworth, Harold McLean, M.B., Ch.M., 1924 (Univ. Sydney), Townsville.
McFadden, Agnes Sophia, M.B., Ch.M., 1923 (Univ. Sydney), Kynuna.
Nye, Leslie John Jarvis, Ch.M., 1918 (Univ. Sydney), Atherton.

Books Received.

AN INTRODUCTION TO PRACTICAL BACTERIOLOGY, by T. J. Mackie, M.D. (Glasgow), D.P.H. (Oxford) and J. E. McCartney, M.D., D.Sc. (Edinburgh); 1924. Edinburgh: E. and S. Livingstone. Crown 8vo., pp. 297. Price: 8s. 6d. net.

DISEASES OF THE HEART, by Dr. Henri Vaquez; 1924. Philadelphia and London: W. B. Saunders Company. Royal 8vo., pp. 743, with illustrations. Price: $8.50 net.

GENERAL SYSTEMATIC BACTERIOLOGY, by R. E. Buchanan, Ph.D.; 1925. Baltimore: Williams & Wilkins Company. Royal 8vo., pp. 597. Price: $6.00 net.

INFECTION, IMMUNITY AND INFLAMMATION, by Fraser B. Gurd, B.A., M.D., C.M., F.A.C.S.; 1924. St. Louis: The C. V. Mosby Company. Royal 8vo., pp. 329. Price: $5.00.

MANUAL OF PSYCHIATRY FOR THE MEDICAL STUDENT AND GENERAL PRACTITIONER, by Paul E. Bowers, M.D.; 1924. London: W. B. Saunders Company. Demy 8vo., pp. 365. Price: $3.50.

PERNICIOUS ANÆMIA AND APLASTIC ANÆMIA, by Arthur Sheard, M.D.; 1924. Bristol: John Wright and Sons, Limited. Royal 8vo., pp. vii. + 94. Price: 7s. net.

THE EFFECTS OF INANITION AND MALNUTRITION UPON GROWTH AND STRUCTURE, by C. M. Jackson, M.S., M.D., LL.D.; 1924. Philadelphia: P. Blakiston's, Son and Company. Royal 8vo., pp. xii. + 616, with 117 illustrations. Price: $8.00.

THE PRACTICE OF PEDIATRICS, by Charles Gilmore Kerley and Gaylord Willis Graves; Third Edition; 1924. Philadelphia and London: W. B. Saunders Company. Royal 8vo., pp. 922, with 150 illustrations. Price: $9.00 net.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xvi.

GOVERNMENT OF TONGA, PACIFIC ISLANDS: Medical Officers (2).

MENTAL HOSPITAL, PARKSIDE, SOUTH AUSTRALIA: Junior Medical Officer.

QUEEN VICTORIA HOSPITAL, MELBOURNE: Medical Superintendent.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429, Strand, London, W.C..

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham Dispensary. Manchester Unity Oddfellows' Medical Institute, Elizabeth Street, Sydney. Marrickville United Friendly Societies' Dispensary. North Sydney United Friendly Societies. People's Prudential Benefit Society. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited Mutual National Provident Club. National Provident Association.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane United Friendly Society Institute. Stannary Hills Hospital.
SOUTH AUSTRALIAN: Honorary Secretary, 12, North Terrace, Adelaide.	Contract Practice Appointments at Renmark. Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Diary for the Month.

MAR. 24.—New South Wales Branch, B.M.A.: Council (Quarterly).
MAR. 25.—Victorian Branch, B.M.A.: Council.
MAR. 26.—New South Wales Branch, B.M.A.: Branch (Annual).
MAR. 27.—Queensland Branch, B.M.A.: Council.
MAR. 31.—New South Wales Branch, B.M.A.: Council.
MAR. 31.—Section of Hygiene and Preventive Medicine, New South Wales Branch, B.M.A.
APR. 1.—Victorian Branch, B.M.A.: Branch.
APR. 7.—Tasmanian Branch, B.M.A.: Council.
APR. 9.—New South Wales Branch, B.M.A.: Clinical Meeting.
APR. 9.—Victorian Branch, B.M.A.: Council.
APR. 14.—New South Wales Branch, B.M.A.: Ethics Committee.
APR. 14.—Tasmanian Branch, B.M.A.: Branch.
APR. 16.—Section of Neurology and Psychiatry, New South Wales Branch, B.M.A.
APR. 21.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
APR. 21.—Tasmanian Branch, B.M.A.: Council.
APR. 22.—Victorian Branch, B.M.A.: Council.
APR. 24.—Queensland Branch, B.M.A.: Council.
APR. 24.—Eastern Suburbs Medical Association, New South Wales.
APR. 28.—New South Wales Branch, B.M.A.: Medical Politics Committee; Organization and Science Committee.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, Sydney. (Telephones: MW 2651-2.)

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad *per annum* payable in advance.